Simulation Models for between Farm Transmission of PRRS Virus in Canadian Swine Herds

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Examiners

Dr. Larry Hammell - Chair

Dr. Cheryl Waldner - External Examiner

Dr. Ian Gardner

Dr. Dan Hurnik

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Date

To my parents, Mina Devi Thakur and Anand Kumar Thakur, wife Nitu Jha Thakur, son Amish Kumar Thakur and daughter Arya Thakur

Abstract

Porcine reproductive and respiratory syndrome (PRRS) is a viral disease of pigs, which affects all production stages and has severe economic consequences for the swine industry. The virus is primarily spread between farms through direct and indirect contacts. A limited number of studies have been carried out to understand the between-farm transmission dynamics of the virus. The objectives of this thesis were to explore the contact structures among swine farms in Canada and to use these contact structures to better understand the pattern and dynamics of between-farm spread of PRRS virus among Canadian swine herds.

Four different studies were designed and implemented to achieve these objectives. The first study used network analysis tools to analyse pig movement data which revealed characteristics of contact patterns between swine herds and suggested a hierarchical structure within the Canadian swine industry, where pigs typically move in a unidirectional manner from one production stage to another. The median in-degree and out-degree for farms in this study was 1 and ranged between 0-26 and 0-10 respectively for the overall network. The degree distributions demonstrated characteristics of a power-law distribution, suggesting the presence of scale-free structure while the size of clustering coefficient suggested presence of small-world structure in the swine movement network. Additionally, high levels of truck sharing between farms were noted in this study, with a typical truck, during the study period, being shared among four different farms. The second and third studies simulated the between farm spread of the PRRS based on the movement of pigs and the sharing of trucks among swine farms, using the North American Animal Disease Spread Model and the network-based models

respectively. These studies provided a means to assess the relative importance of direct and indirect contact via truck sharing on between farm spread of PRRS virus. By including the transmission by trucks in the model, the median number of infected farms increased by 18% and the median epidemic size increased by 44% in the spatial model. Furthermore, with the addition of trucks in the model, the hierarchical structure of the industry was significantly altered and multidirectional disease spread was observed. On the other hand, the network-based models assessed the impact of scale-free, small-world and random network structures on the between farm spread of PRRS virus and demonstrated the influence these network structures can have on the spread of the virus. The spread on scale-free networks resulted in the smallest stochastic die-out percentage with highest epidemic sizes compared to spread on small-world or random networks. Similarly, the incorporation of transmission by trucks in the model had the highest impact on small-world and random networks, where the epidemic size doubled, compared to scale-free networks, where it increased by 20-29%. Given the importance of transmission of the virus via truck (e.g. indirect contacts) identified in the previous studies, the last chapter aims at (i) quantifying the likelihood that a pig transport truck shared among farms could remain contaminated with PRRS virus at the end of Day 1 and to (ii) evaluate the efficacy of commonly used cleaning and disinfection protocols in eliminating the virus from these trucks. The results of this study suggested, when no cleaning and disinfection protocol is applied, that it is moderately likely that the truck could become contaminated and remain infected with the PRRS virus (mean probability ranged between 0.338-0.352, when the truck was shared between two farms), and that this risk marginally increased with an increase in the number of farms the truck was

shared among. This final study also suggested that once contaminated, most of the contaminated trucks would likely remain infected for more than one day.

The studies presented in this thesis have not only provided a clearer insight into the pattern of contacts between farms, and the impact these contacts can have on PRRS virus spread, but have also highlighted the importance of including data on the sharing of trucks among farms, since trucks will tend to connect farms which would otherwise share no connection. Moreover, the studies in this thesis have reinforced the importance of the proper cleaning and disinfection of trucks between successive shipments, as the findings presented here suggest that with an increasing level of truck sharing between farms, shared trucks are likely to remain contaminated with the virus and sharing of trucks significantly increased the risk of between farm spread of PRRS virus. Not only do the shared trucks have a high probability of becoming contaminated with the virus, but once contaminated, they are likely to remain infected for a comparatively long period particularly in the absence of adequate disinfection. It should be noted that the pig movement data used in this study was not very recent and consisted of movements reported for only four months time period. Additionally, the described models could not be validated due to unavailability of data is another noteworthy limitation of the studies described in this thesis.

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List of Abbreviations

ABM	Agent Based Model
AIAO	All in all out
ARC&E	Area regional control and elimination
CI	Confidence interval
CrI	Credible Interval
DPI	Days post infection
FinishingA	All in all out finishing farms
FinishingC	Continuous flow finishing farms
FMD	Foot and Mouth Disease
IQR	Inter Quartile Range
KS	Kolmogorov–Smirnov test
McRebel	Management Changes to Reduce Exposure to Bacteria to Eliminate Losses
NA	Network analysis
NAADSM	North American Animal Disease Spread Model
NurseryA	All in all out nursery farms
NurseryC	Continuous flow nursery farms
GSC	Giant strong component
GWC	Giant weak component
ORF	Open Reading Frame
PED	Porcine Epidemic Diarrhea
PRRS	Porcine Reproductive and Respiratory Syndrome
QAP	Quadratic assignment procedure
SF	Scale-free
SI	Susceptible Infectious
SIS	Susceptible Infectious Susceptible
SW	Small-world
UK	United Kingdom
USA	United States of America

Chapter 1 Introduction

1.1 PRRS Virus

Porcine Reproductive and Respiratory Syndrome (PRRS) is a contagious viral disease affecting all production stages of swine and is considered as one of the most prevalent disease of swine in the world (Lunney et al., 2010). PRRS has the highest economic impact on the swine industry, accounting for an annual loss of $560 million to US swine industry (Neumann et al., 2005) and $130 million to Canadian swine industry (Mussell, 2010). Some of the characteristics of PRRS include: late-term abortions, still-births, mummified foetuses and weak piglets in breeding herds, an increased mortality rate in piglets and respiratory disease, poor growth performance and mortality in growing pigs (Nodelijk, 2002).

PRRS virus is a small, enveloped, single stranded positive-sense RNA virus, which belongs to the order *Nidovirales* and family *Arteriviridae* (Murtaugh et al., 1995). The divergent evolution of the virus on two continents was also reflected genetically, as viruses from the two continents had only around 55-70% nucleotide similarity, and led to further classification of the virus into two distinct genotypes: Type I, as the European genotype and Type II, as the North American genotype (Wensvoort et al., 1992; Murtaugh et al., 1998). Genetic diversity among the strains of the virus relating to the same genotype is another concern for the control of the virus, as the virus mutates and or recombines continuously (Chang et al., 2002). It is estimated that the nucleotide substitution rate for PRRS virus ranges between 4.7 to 9.8X 10^{-2}/site/year, which is the highest substitution rate calculated for any RNA virus (Jenkins et al., 2002; Hanada et al., 2005).

As PRRS virus is an enveloped virus, its survival outside the host is affected by ambient temperature, relative humidity and pH (Zimmerman et al., 2012). The virus can remain infective in the environment for around a week at 21^0C, however the infectivity of the virus is shortened to around a day at 37^0C and to around 20 minutes at 56^0C. However, the virus remains stable for long durations at lower temperatures, remaining stable for around a month at 4^0C and for four months or even longer, at temperatures lower than -20^0C (Benfield et al., 1992).

The primary target cells for PRRS virus are the cells of monocyte / macrophage lineage. The virus replicates in specific subsets of differentiated macrophages in lungs, lymphoid tissues and placenta (Van Breedam et al., 2010). Viremia in some pigs starts as early as 12 hours, and in all pigs by 24 hours post exposure. Experimental studies have shown that animals start shedding the virus after 2 days post infection (Chand et al., 2012; Le Potier and Rose, 2012). Highest viral titre is evident during 7-14 days post inoculation (DPI) in serum, lung and lymph nodes. After reaching the peak viral titre, the acute phase of viremia may subside by 28 DPI and most pigs may not be viremic beyond 28 days. However, following the initial clearance of viremia, the infected animals may still harbour the virus in lymphoid tissues for extended periods of time exhibiting persistent infection with the virus. Viremia may periodically re-appear with replication of the virus in lymph nodes (Allende et al., 2000; Boddicker et al., 2012) and virus has been detected by virus isolation for several months (up to 132-157 DPI) after inoculation (Wills et al., 1997a; Horter et al., 2002; Rowland et al., 2003).

The PRRS virus is present in serum and in many tissues as well as secretions and excretions of the infected animals. PRRS virus has been isolated from nasal secretions,

oral fluids, semen, milk, urine and feces of infected animals (Wills et al., 1997c; Bierk et al., 2001). Infected animals may shed virus in saliva for up to 42 DPI, in nasal secretions up to 38 DPI, in urine up to 28 DPI and in feces up to 35 DPI (Prieto and Castro, 2000).

Several routes of exposure leading to infection to PRRS virus have been outlined for susceptible pigs: intranasal, intramuscular, oral, intrauterine and vaginal. Within a herd, PRRS is primarily transmitted via close contact between susceptible and infectious pigs, mainly through nose-to nose contact or by contact with urine and feces of infected animal (Albina, 1997). Transplacental transmission to foetuses during mid to late gestation and transmission of the virus from infected sows to suckling piglets have also been documented (Zimmerman et al., 2012). Transmission via artificial insemination, when using virus contaminated semen is also well established (Yaeger et al., 1993). In addition, several husbandry practices like tail docking, tattooing and inoculations may also lead to transmission of the virus, when contaminated tools or needles are used (Otake et al., 2002b; Zimmerman et al., 2012).

The well agreed upon mechanisms for between farm transmission of PRRS virus are via the introduction of infected animals, through the introduction of infected semen and via aerosols (Yaeger et al., 1993; Mousing et al., 1997; Weigel et al., 2000; Mortensen et al., 2002; Dee et al., 2010; Otake et al., 2010). In addition, vehicles used for the transportation of pigs, and associated fomites (boots, coveralls, bedding materials etc.), has been implicated for spread of the virus over long geographical distances. This was demonstrated in a series of transmission experiments using contaminated vehicles and fomites (Dee et al., 2002a; Otake et al., 2002c; Dee et al., 2004b; Holtkamp et al., 2010), where the vehicles itself can act as a mechanical carrier of the virus or susceptible

animals can get infected when transported in a contaminated vehicle. Spread of PRRS virus to PRRS virus free distant herds, via transportation, have also been reported from the USA (Torremorell et al., 2004).

Local transmission or area spread of PRRS virus is accepted, as a mechanism for between farm spread of the virus, by most of the studies. However the distance over which the virus can spread from the initial source farm is inconsistent among studies. Proximity to infected herds is one of the risk factors for PRRS virus infection, and the risk of a naive herd becoming infected with the virus increases with the density of PRRS virus positive herds in the neighbourhood and the risk decreases with increasing geographical distance between herds (Mortensen et al., 2002; Zimmerman et al., 2012). Area spread of the virus by aerosols within 150 metres has been reported from an experimental study (Otake et al., 2002a). Le Potier and colleagues reported that 45% of herds suspected to have acquired infection via aerosol were located within 0.5 km of the initial source herd and only 2% of the herds were 1 km away from the initial herd. (Le Potier et al., 1997). The dependence on geographical distance for airborne transmission of the virus may be related to the strain of the virus. As one study with PRRS virus strain 1-8-4 had believed to spread up to 9.1 km, while strains 1-8-2 and 1-26-2 could not be detected beyond 2 km (Otake et al., 2010). Weather conditions may also play role in spread of the virus via aerosol, including factors such as temperature, relative humidity, wind velocity and direction and precipitation (Dee et al., 2010). Some other work has been published describing the genetic similarity of PRRS virus from infected farms, which were not in close geographical proximity (Goldberg et al., 2000; Mondaca-Fernández et al., 2006; Lambert et al., 2012a). These works suggested a potential long-

distance spread of the virus due to the movement of infected pigs and other forms of indirect contact between distant farms. Similarly, one study from USA reported that 17% of the infected herds were suspected to have introduced the PRRS virus via contaminated transport (Torremorell et al., 2004).

Some of the well-recognized risk factors for infection of farms with PRRS virus are the size of the herd, the practice of replacing animals from unknown sources, increase in the number of times replacement animals are introduced to the farm, absence of quarantine for replacement animals, and density of farms or proximity to other farms (Albina, 1997; Le Potier et al., 1997; Mousing et al., 1997; Mortensen et al., 2002; Holtkamp et al., 2010).

Several strategies for effective prevention, control and elimination of PRRS virus has been published. These strategies include: (i) measures that can limit the introduction of new pathogens to the farm, such as application of high external biosecurity standards, (ii) measures that can control ongoing infection on the farm, such as McRebel piglet management, gilt acclimatization, and vaccination and (iii) measures for elimination of the virus from the farm, such as herd closure, depopulation/repopulation and rollover (McCaw, 2000; Dee et al., 2004c; Corzo et al., 2010).

External biosecurity measures that potentially can limit the introduction of PRRS virus into a herd rely on the following practices: introduction of animals from trusted sources or from PRRS free herds, application of quarantine of 30 days for incoming animals, use of clean and disinfected equipment, regular cleaning and disinfection of transportation vehicles used for shipment of pigs, application of Danish entry system for people,

proper handling of dead stock and control of other potential mechanical vectors, as well as filtration of incoming air (Dee et al., 2004c; Dee et al., 2005a; Lambert and Dallaire, 2009; Pitkin et al., 2009).

Elimination of PRRS virus from contaminated trucks requires rigorous cleaning and disinfection. Several standard protocols have been developed for cleaning and disinfection of transport vehicles used for shipment of pigs to effectively get rid of the PRRS virus (Dee et al., 2004a; Dee et al., 2004b; Dee et al., 2004c; Dee et al., 2005a; Dee et al., 2005b). However, field studies have shown that nearly one third of such vehicles are not properly cleaned and disinfected between successive shipments (Lambert et al., 2012b), partly due to the high cost associated with effective cleaning and disinfection, therefore increasing the likelihood for spread of the PRRS virus via transportation trucks.

Breeding farms with a target to eliminate the virus from the premises had little success and had recurrent recirculation of the virus if they did not continually incorporated McRebel management practices (Polson et al., 2010). The McRebel concept stands for "Management Changes to Reduce Exposure to Bacteria to Eliminate Losses". Incorporation of this practice in disease control protocol includes measures such as limiting cross-fostering to a minimum, eliminating poor performing non-responsive pigs, changing needles between litters or pens and taking extra care of the smallest pigs (Corzo et al., 2010).

Gilt acclimatization is a practice to induce immunity in replacement gilts by exposing them to a circulating strain of virus before they are replaced as breeding stock (Batista et

al., 2002). Gilts are exposed to circulating virus either by inoculating serum or tissue scrapings from viremic nursery pigs, or to expose them to viremic nursery pigs and allow the virus to transmit via contact.

Inactivated, as well as modified live virus vaccines, have been commercially available and used in breeding animals, replacement pigs and grower pigs for the control of PRRS virus (Corzo et al., 2010). However, the high heterogeneity in the genetic makeup of PRRS virus isolates is likely the main hindrance towards effective control of the virus by use of commercial vaccines, as the induced immunity to one strain of virus is not always cross protective or is only partially protective to a different strain, even if the viruses belong to the same genotype (Meng, 2000; Mateu and Diaz, 2008; Kimman et al., 2009).

Eliminating PRRS virus from an infected herd via test and removal has also been documented (Corzo et al., 2010). It is based on serological test for PRRS virus antibodies or detection of viral RNA in the serum and if one of these tests is positive, the animal is immediately culled from the herd. The disadvantage of this method is the cost of testing and the cost of removal of a productive animal. In addition, the test accuracy may be critical as false positive animals may be removed while false negatives may still be present in the herd (Dee et al., 2001; Dee, 2004). The tests commonly applied for are ELISA using commercial test kits (Idexx-ELISA) to detect the viral antibody, which is claimed to have very high specificty (Nodelijk, 2002) and Reverse-transcription polymerase chain reaction (RT-PCR) to detect PRRS virus RNA in tissue, serum and several bodily secretions and excretions, which has very high sensitivity.

The whole herd depopulation and repopulation method is based on removal of all breeding and/or growing pigs from the farm, cleaning and disinfecting the facilities, allowing certain down time before restocking the farm with PRRS virus negative pigs. This method is highly effective in eliminating the virus from the facilities, but a whole herd repopulation is very expensive. However, one important advantage of this method is that other pathogens will simultaneously be eliminated from the herd (Corzo et al., 2010).

Herd Closure and rollover is one of the most widely used methods for eliminating the PRRS virus from breeding herds and has been reported as the least expensive method for the elimination of the virus (Corzo et al., 2010). This method consists of avoiding introduction of replacement gilts into the herd for at least six months accompanied with removal of seropositive animals from the herd (Torremorell et al., 2003). Success of herd closure is enhanced if all the breeding animals in the herd are acclimatized at the same time, with the circulating strain of the virus, before herd closure is initiated.

To avoid reinfection from neighbouring farms, after elimination or control of a disease, a regional integrated approach of all the farms and disease control managers in the geographical region is required (Corzo et al., 2010). Recently, Sweden has reported successful elimination of PRRS virus through a coordinated cooperation between the swine industry, veterinarians and government authorities. Similar approaches to control the virus from a geographical region have been initiated in several countries. In North America, swine farms in several geographical regions are voluntarily participating in Area Regional Control and Elimination (ARC&E) project (Corzo et al., 2010). The impact of such projects on regional control of PRRS virus is still to be evaluated.

1.2 Overview of modelling methods applied to understand the between-farm spread of PRRS virus

1.2.1 Network Analysis

The trade of live animals, which requires movement of animals between premises, is a key economic activity in many livestock industries. However, such movement of animals can also be instrumental in the long distance spread of infectious agents, as was evident during the 2001 Foot and Mouth disease outbreak in the United Kingdom (Fèvre et al., 2006; Ortiz-Pelaez et al., 2006). Movement of animals, which brings susceptible animals into direct or indirect contact with infectious agents, is one of the major pathways for the introduction and spread of infectious agents between premises (Bigras-Poulin et al., 2007).

Besides movement of infected animals between farms, studies have shown that vehicles used in the shipment of animals between farms may also influence the indirect or mechanical spread of infectious agents such as FMD or PRRS viruses (Dee et al., 2002b; Alexandersen et al., 2003; Dee et al., 2004b). The first published study discussing the specific risks modern transportation of livestock can have on disease spread dates back to 1970, in which four key components that can augment the potential of infectious disease spread were identified: transport vehicles, infectious animals, travel route and travel time (Hansen Jr, 1970). Trucks used in the shipment of animals can become contaminated when shipping infected animals which increases the risk of spread of infectious disease to naive farms upon subsequent use of such trucks (Bigras-Poulin et al., 2007; Smith et al., 2012), particularly if trucks are not cleaned between successive uses or are poorly cleaned (Bottoms et al., 2012a; Lambert et al., 2012b). Sharing of trucks between farms for shipment of animals may connect farms that are not connected

through direct animal movement. Recent studies from Denmark, France and the UK have demonstrated high levels of truck sharing between swine farms in the shipment of pigs (Bigras-Poulin et al., 2007; Rautureau et al., 2012a; Smith et al., 2012).

Commercial swine production in North America has undergone a massive transformation towards intensive multi-site production systems, in which various age groups of pigs are grown at different geographical locations. This in turn requires large numbers of growing pigs and breeding animals to be moved from one site of production to another on a regular basis. The major benefit of this production system is an increase in efficiency with specialization of production, while at the same time the health status of many swine herds has improved dramatically due to improved biosecurity and the effective implementation of all-in-all-out (AIAO) policies (Harris, 2008; Key and McBride, 2010). However, with the increase in the number of movements between farms, connectivity between farms increases posing an increased threat in terms of the spread of infectious diseases.

Network analysis (NA) is based on graph theory and offers an analytical framework to explore the pairwise contact structures, as well as the patterns and implications of these contact structures between entities in a population (Wasserman and Faust, 1994). The increase in availability of animal movement data has seen an increased use of NA tools in veterinary epidemiology to unravel the relationships among farms, markets and dealers in the livestock industry.

Two review papers (Dubé et al., 2009; Martínez-López et al., 2009) provide an excellent summary of the concepts of NA in the context of their use in the study of animal

movements. A number of published studies have also described, in detail, the contact patterns that exist among farms for specific livestock industries in different geographical locations (Bigras-Poulin et al., 2006; Bigras-Poulin et al., 2007; Natale et al., 2009; Lockhart et al., 2010; Volkova et al., 2010; Nöremark et al., 2011a; Rautureau et al., 2011; Rautureau et al., 2012b; Smith et al., 2012; Büttner et al., 2013a; Büttner et al., 2013c; Dorjee et al., 2013).

Most studies broadly characterise these animal movement networks as having two distinct topological structures: those being small-world and scale-free network characteristics (Webb, 2005; Bigras-Poulin et al., 2006; Kiss et al., 2006b; Bigras-Poulin et al., 2007; Lockhart et al., 2010; Dubé et al., 2011a; Rautureau et al., 2011, 2012a; Büttner et al., 2013b; Dorjee et al., 2013). The small-world and scale-free topologies are also evident in many other real world networks, such as for the World Wide Web, for the network of electricity grids, or for citation networks for academic papers (Amaral et al., 2000; Barabási et al., 2000). The small-world networks tend to have relatively high clustering coefficients and shorter average path length than would be the case for a random network of the same size (Watts and Strogatz, 1998; Watts, 2003). Small-world networks have sub-groups or clustering of individuals, in which the probability that two nodes of the network will be connected increases if they have some common connection and these clusters/sub-groups are further connected with other nodes of the network by some long-range connection. Hence, in small-world networks, even though individuals in the network may not be directly connected, they can be reached in fewer steps via these long-range connections. In a scale-free network, many individuals in the network have few connections and a few individuals have a relatively large number of

connections, such that the distribution representing the number of connections between individuals is right-skewed with a long tail and follows a power-law distribution (Barabási and Albert, 1999).

Knowledge of the network structure connecting farms can provide insights on probable patterns of infectious disease spread in the population under study, and can also be helpful in effectively managing surveillance and disease control programs (Kiss et al., 2006b; Martínez-López et al., 2009; Dubé et al., 2011b; Nöremark et al., 2011b). In scale-free networks, farms with a large number of connections will tend to act as "hubs". Once these hubs become infected the disease can spread rapidly to other farms in the network. However, the spread gradually slows as the farms connected to the hubs become infected (Shirley and Rushton, 2005a; Ortiz-Pelaez et al., 2006; Dubé et al., 2009). Similarly, for targeted surveillance or efficient disease control, strategically targeting farms with a higher number of connections (i.e. hubs) may yield better outcomes than simply selecting random farms of the population (Martínez-López et al., 2009; Nöremark et al., 2011b). On the other hand, disease spread may be comparatively slow in a small-world network, but it can potentially spread to topologically distant farms in the network and the infection may persist longer in this type of network when compared to scale-free or random networks. However, the comparative size of any epidemic in a small scale network is likely to be smaller than would typically be the case for random or scale-free networks (Rahmandad and Sterman, 2008; Lockhart et al., 2010).

1.2.2 Simulation modelling approaches for infectious diseases

Recently, computer simulation models have been widely used to explore the pattern and dynamics of infectious disease spread and these models have provided important insights on the spread of diseases, such as severe acute respiratory syndrome (SARS) (Lipsitch et al., 2003; Lloyd-Smith et al., 2003; Gumel et al., 2004) and the foot-and-mouth disease (FMD) outbreak of 2001 in the United Kingdom. Simulation models allow us to explore thousands of artificially designed experiments and 'what if' scenarios pertaining to several disease outbreak scenarios. Due to economical, logistical and welfare concerns, similar experiments could not be conducted under real world conditions (Keeling and Rohani, 2008; Vynnycky and White, 2010). Disease spread models are designed to represent real world situations in a simplified mode and through these *in silico* experiments, modellers can explain the behaviour of a complex biological system. Similarly, simulation models are useful in determining the impact of key parameters on the dynamics of disease spread as well as the efficacy of different intervention strategies in controlling disease spread or to support informed policy decisions (Morris et al., 2001; Riley et al., 2003; Taylor and Gate, 2003; Kiss et al., 2006a; Francis et al., 2010).

Several types of models, ranging from simple deterministic differential equation models, also known as system dynamics or compartmental models (Mills et al., 2004; Arino et al., 2008; Brauer, 2008) to more complex, stochastic, individual or agent based models (Rahmandad and Sterman, 2008; Carpenter and Sattenspiel, 2009; Dürr et al., 2013; Patyk et al., 2013) have been used to study infectious diseases in human and animal populations. Some agent based models explicitly incorporate contact network structure

among the individuals in the population (Eames and Keeling, 2002; Ayyalasomayajula et al., 2008b; Chao et al., 2010; Rahmandad et al., 2011) while some others assign a random contact based on the relative geographical distance among the individuals (Garner et al., 2011; Taylor et al., 2011; Dürr et al., 2013; Patyk et al., 2013). For the models that incorporate network structure, the direct contact between individuals of the population is limited to only those individuals that are connected as per the construction rules of the specified network structure (Eames and Keeling, 2002; Ayyalasomayajula et al., 2008b; Chao et al., 2010; Rahmandad et al., 2011). On the other hand, for models such as NAADSM, each individual, farm has a discrete spatial location; however no contact network structure is imposed, and so farms within a contact group is allowed to contact any other farm randomly. These type of models are called "spatially-explicit" models throughout this thesis. Additionally, for spatially-explicit models, disease spread among individuals is also influenced by spatial distance between individuals (Harvey et al., 2007).

Most traditional system dynamics models consider the population at risk as the number of units existing in each state at a given time and use differential equations to estimate the transition of populations from one state to another (Rahmandad and Sterman, 2008); most of these models fail to account for the chance nature of epidemic spread (randomness/ stochasticity) as well as heterogeneity in contact patterns that exist among individuals within a population (Dangerfield et al., 2009). Agent based models (ABM), on the other hand, not only allow flexibility to incorporate individual-level attributes such as age, sex, production type, or farm size, as well as spatial locations of the individuals, but can also account for randomness to select parameter values or to select

individuals in the model. Moreover, individuals in the population can be traced throughout the simulation in terms of their infection status and a record of the contacts for each individual can be maintained. This allows for a more complete evaluation of targeted surveillance and intervention strategies. However, the added benefits of the ABMs come at a price, not least of which being that they are more computationally intensive and therefore time consuming. In addition, the increased granularity of the model requires more detailed individual-level data, which is often sparse and can make it difficult to parameterize such models; while the added randomness can create difficulties in performing sensitivity analysis and ascertaining the impact of various parameters on model outcomes (Brauer, 2008; Gojovic et al., 2009).

A number of software platforms have been developed to implement models that can assess the spread and control of highly contagious animal diseases; including AusSpread (Garner and Beckett, 2005) InterSpread Plus (Stevenson et al., 2013b) and the North American Animal Disease Spread Model, NAADSM (Harvey et al., 2007).

The NAADSM is an agent based, farm-level, stochastic, spatially explicit, state-transition modelling platform that allows for the simulation of infectious disease spread in populations via direct contact (through movement of infected animals), indirect contact (through the movement of people, fomites or sharing of equipment), aerosol and local area spread. The epidemiological unit of interest within NAADSM is the herd or farm, which is a group of animals, managed together at a single geographic location, and these are defined by their actual physical location in a geographical region. It is flexible, as the users can define the probable contact groups in which disease can spread (e.g. between sow and nursery farms or nursery and finishing farms) and allows for user-

established disease parameters to define model behaviour. Each unit is initially assigned attribute data which include a unique unit ID; the type of farm (e.g. dairy, beef, swine, etc.); farm size; location of the farm (longitude and latitude of the farm); and disease transition state. Disease spread between farms is influenced by rates of direct and indirect contact, relative locations, and distances between farms. An infected farm progresses from one disease state to another over time. The model can predict the total number of infected premises without any intervention applied, or can also evaluate the impact of a number of different disease intervention strategies, such as: quarantine; movement control; vaccination; depopulation and zoning on the spread of the disease (Harvey et al., 2007). This platform was originally developed to simulate the spread and control of contagious animal diseases (e.g. FMD) between farms of the same or different species and production types. Recently, NAADSM has been used to explore the dynamics of spread of other infectious agents such as the highly pathogenic Avian Influenza in poultry, the spread of influenza between human and swine populations, and to evaluate eradication strategies for pseudo rabies (Ketusing et al., 2012; Patyk et al., 2013; Dorjee et al., 2014).

Network- based models, where either a theoretical network structure or empirical network structures between individuals in the population are explicitly incorporated into the ABM, have recently been extensively used as these models can impart additional realism in terms of contacts between individuals (Riley et al., 2003; Eubank, 2005; Shirley and Rushton, 2005b; Kao et al., 2006; Kiss et al., 2006a; Kiss et al., 2006b; Rahmandad and Sterman, 2008; Vernon and Keeling, 2009). For several infectious diseases, including PRRS, the pathogen is spread mainly by direct or indirect contact

between individuals. Thus, disease is spread by a network of contacts (via movement of infectious animals) such that the probability of spread of infection is limited to a finite set of susceptible contacts in contrast to the assumption of mass-action models in which every susceptible individual in the population has a certain probability of becoming infected (Keeling, 2005). As individuals have contacts only with a finite set of other individuals in the population, network-based models with scale-free or small-world networks more closely mimic the system modelled compared to models with contacts randomly assigned between individuals. The increase in use of these recent modelling approaches is facilitated by the advancement in high-performance computing resources, availability of advanced modelling software, as well as an increase in the availability of data required to parameterize these models (Morris et al., 2001; Rahmandad and Sterman, 2008; Vernon and Keeling, 2009; Stevenson et al., 2013b).

1.2.3 Bayesian approach for probabilistic risk assessment

Probabilistic risk assessment is widely applied to many domains in science, technology and medicine including: aerospace, military, nuclear energy, chemical processing, human and animal health (Bedford and Cooke, 2001). In veterinary epidemiology, this approach has been used to assess the entry of pathogens through trade and importation of animals or animal products, as well as to assess the microbiological risk through the consumption of contaminated food products (Notermans and Mead, 1996; Zepeda et al., 2001). However these methods are equally applicable to other disease-related decision making areas, such as in surveillance or disease control programs (MacDiarmid and Pharo, 2003).

Probabilistic risk assessment models can be implemented using one of two distinct stochastic modelling techniques: Monte Carlo simulation or Bayesian inference. Monte Carlo simulation is intuitive, relatively easy to implement, can simulate complex systems with all kinds of probability distributions and with correlated parameters, and because of this is widely used and accepted. However it is unidirectional as information cannot be propagated from downstream component of the model, and the model is not interactive as the data and parameters of the model are not interlinked or as the parameters estimated from the data for one node of the model does not influence the parameters estimate for other nodes of the model, which were estimated from separate data sources. These models are also difficult to update as new information becomes available and do not allow for backwards reasoning (Smid et al., 2010).

On the other hand, the Bayesian approach allows for the incorporation of uncertainties, as well as information from different sources in the model; for example, knowledge from experts can be incorporated as priors in the model (Czado and Brechmann, 2014). Some additional advantages of using Bayesian approach include: the parameters of the model interact as knowledge from one part of the model migrates to other parts of the model, parameters in the model can be continuously updated as new information becomes available, model validation is comparatively easier as it allows for 'backward' reasoning, and a graphical interface simplifies model presentation to non-experts (Smid et al., 2010; Greiner et al., 2013). In addition, it allows the assumption of conditional dependence between nodes required in classical risk assessment to be relaxed, thus permitting the estimation of joint distributions at nodes that are conditionally independent through the use of Bayesian belief networks (Albert et al., 2008). Bayesian

networks are a graphical representation of a model with a set of statistical variables that define the model and their probabilistic dependencies. The network is usually represented using a directed acyclic graph in which nodes represent the variables and the relationships between variables are represented by directed arcs. The absence of an arc between any two nodes indicates absence of dependency between these variables. Any relationship in the network is expressed in terms of probabilities that describes the strength of the relationship between the variables represented in the qualitative component of the model (Nielsen and Jensen, 2009). A Bayesian network uses Bayes' rule (Grether, 1980) to estimate the posterior distributions across nodes based on a set of given prior knowledge about the variables together with the observed data.

Several studies have utilized the Bayesian approach to assess the risk for exposure to contaminated food with microbes or to assess the risk of food-borne illness (Hald et al., 2004; Delignette-Muller et al., 2006; Albert et al., 2008). Delignette-Muller and colleagues have evaluated the risk of exposure to *Listeria monocytogenes* in cold smoked salmon, where they describe the effect of time and temperature on bacterial growth, by taking into account the variability between strains of Listeria and between several salmon products (Delignette-Muller et al., 2006). Additionally, this study has also discussed the usefulness of the Bayesian approach in estimating and updating posterior probabilities through Bayesian inference by taking into account information available from expert knowledge and experimental data (Delignette-Muller et al., 2006). Similarly, Albert et al. (2008) assessed the risk of Campylobacter infection in humans, due to consumption of chicken meat, and discussed how the Bayesian approach can first be utilized to theoretically represent complex systems and then demonstrated its ability

to efficiently spread any new information throughout the Bayesian network. They incorporated information from 'downstream' components of the model, which then propagate throughout the network and allow for back-calculation of posterior probabilities associated with unobserved nodes (Albert et al., 2008). Additionally, this study has suggested that Bayesian approaches can be used for the prediction or evaluation of associated risks for a set of different behaviours, such as home consumption of chicken (Albert et al., 2008). Moreover, another study (Hald et al., 2004) has quantified the contribution of each of the major animal-food sources to human salmonellosis and this study included prior information for several parameters, such as that accounted for the presumed but unmeasured differences with respect to serotypes and food sources related to human salmonellosis. The same study demonstrated that the estimates of the model parameters could be improved over time by continuously updating the model as new information becomes available from observational studies. It was also demonstrated that risk estimates can be obtained for very specific "what if" scenarios and models (Hald et al., 2004). As such, the incorporation of Bayesian Belief Networks into the risk assessment process can become a powerful tool for risk managers.

1.3 Thesis Objectives

In Canada, there are a limited number of studies describing direct and indirect contact patterns between swine farms. Similarly, the impacts of direct contact (via movement of infected pigs) and indirect contact associated with the movement of animals (via sharing of trucks between farms) on between-farm spread of PRRS virus has not been evaluated

for Canadian swine herds. Swine producers and industry experts in Canada are concerned that the sharing of trucks may be influencing between-farm spread of PRRS virus (http://www.opic.on.ca/biosecurity-resources/transportation). In a separate study in the USA, it was suspected that 17% of infected herds had introduced the PRRS virus via contaminated transport (Torremorell et al., 2004). However, there have been no studies that have quantitatively assessed the risk of PRRS virus contamination as a result of truck sharing.

Thus, the main research questions of interest in this dissertation were: (i) What type of contact pattern exists between swine farms in Canada? (ii) What is the role of transportation trucks in connecting farms that do not share shipment of animals? (iii) What is the likely impact of these direct (movement of animals) and indirect contacts (sharing of trucks between farms) on between-farm spread of PRRS virus? And (iv) how likely are these trucks to become contaminated with the PRRS virus and to remain infected thereafter?

The research presented in this dissertation utilized data collected for a pilot pig traceability project in four regions of Canada from July 1 to November 3, 2004. The data consisted of information on between-farm movement of pigs in these regions. The second chapter of this dissertation provides an analysis of swine movement between farms and describes the characteristics of the contact network of swine farms in these four regions of Canada. In the third and fourth chapters, the contact rates between farms derived from the first chapter and from the swine movement data were used along with some other PRRS virus related parameters (from published literature or experts' judgement) to simulate the between farm spread of PRRS virus in Canadian swine

herds. The third chapter included spatial location of swine farms without imposing network structure for contacts between farms, while the fourth chapter evaluated the impact of perceived contact network structure among swine farms on spread of PRRS virus. In the final substantive chapter, data are incorporated from different sources (swine movement data, published studies and experts' judgement) to quantify the likelihood that shipment trucks will be contaminated with PRRS virus.

The specific objectives of this research are addressed within the main chapters of the thesis as follows:

1. To describe farm-to-farm contact patterns in swine movement and the sharing of trucks between swine farms, in four Canadian regions. In addition to describing these patterns using Network Analysis tools, various contact parameters were obtained for use in network-based simulation models applied to infectious disease spread in Canadian swine populations. (Chapter 2)

2. To develop a model to simulate the between-farm spread of PRRS virus in Ontario swine farms via direct (animal movement) and indirect (sharing of trucks between farms) contacts using the NAADSM framework, and to describe and compare the patterns of outbreak under a range of scenarios. (Chapter 3)

3. To develop a network-based simulation model for the between-farm spread of PRRS virus that could be used to assess the impact of various network structures on between-farm transmission of PRRS virus. (Chapter 4)

4. To quantify the likelihood that a truck used for the shipment of pigs would be infected with PRRS virus, and to evaluate the efficacy of cleaning and washing protocols in eliminating the virus from these trucks, using a Bayesian risk analysis approach. (Chapter 5)

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Chapter 2 Analysis of swine movement in four Canadian regions: Network structure and implications for disease spread

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2.1 Abstract

Direct and indirect contacts among animal holdings are important in the spread of infectious diseases. The objectives of this study were to describe networks of pig movements and the sharing of trucks used for those movements between swine farms in four Canadian regions using network analysis tools and to obtain contact parameters for infectious disease spread simulation models. Four months of swine movement data from a pilot pig traceability program were used. Two types of networks were created using three time scales (weekly, monthly and the full study period): one-mode networks of farm to farm direct contact representing animal shipments and two-mode networks representing the sharing of trucks between farms. Contact patterns among farms were described by estimating a range of relevant network measures. The overall network neglecting the four regions consisted of 145 farms, which were connected by 261 distinct links. A total of 184 trucks was used to transport 2043 shipments of pigs during the study period. The median in- and out-degree for the overall one-mode network was 1 and ranged from 0-26 and 0-10, respectively. The overall one-mode network had heterogeneous degree distribution, a high clustering coefficient and shorter average path length than would be expected for randomly generated networks of similar size. On average, one truck was shared by four farms in the overall network, or by three farms when considered the monthly and weekly networks. Degree distribution of the two-mode overall network demonstrated characteristics of power-law distribution. For more than 50% of shipments on any given day, the same truck was used for at least one other shipment. Findings from this study are in agreement with previous work, which suggested that swine movement networks exhibit small-world and scale-free topologies.

Furthermore, trucks used for the shipment of pigs can play an important role in connecting otherwise unconnected farms and may increase the spread of disease.

Keywords: swine, movement, network analysis, two-mode network, infectious diseases

2.2 Introduction

The movement and trade of live animals constitute major economic activities within the livestock sector. However, movements, where susceptible animals are brought into direct or indirect contact with infectious agents, pose a significant risk for spreading disease between farms. The movement of animals can be pivotal in spreading infectious agents to distant geographical locations, as was noted during the 2001 Foot and Mouth disease outbreak in the UK (Fèvre et al., 2006; Ortiz-Pelaez et al., 2006). Movement of animals is one of the major pathways for introduction and spread of infectious agents between livestock premises. Therefore understanding contact structures and trade patterns within livestock industries can assist epidemiologists in unravelling the potential impact of animal movement on disease spread (Bigras-Poulin et al., 2007).

In addition to the risk of transmission of diseases via the movement of infected animals, vehicles used in animal transportation can also be involved in the indirect or mechanical spread of infectious agents such as FMD or PRRS viruses (Dee et al., 2002b; Alexandersen et al., 2003; Dee et al., 2004b). The sharing of trucks between farms for the shipment of pigs may increase the risk of infectious disease spread (Bigras-Poulin et al., 2007; Smith et al., 2012), due to poor cleaning and disinfection of trucks (Bottoms et al., 2012a; Lambert et al., 2012b). Investigation of the level of truck sharing among

farms is thus important in understanding linkage and potential disease spread between otherwise unconnected farms.

Network Analysis (NA) provides an analytical framework to study pair-wise relationships as well as the patterns and implications of these relationships among entities (Wasserman and Faust, 1994). Advances in network theory and computing power together with increased availability of animal movement data have provided new opportunities to explore contact structures within the livestock industry, including among farms, markets and dealers. In recent years NA has increasingly been used in veterinary epidemiology. Two reviews (Dubé et al., 2009; Martínez-López et al., 2009) have summarized the concepts of NA in the context of exploring networks of animal movements. A number of studies have been published which describe the contact patterns among farms for specific livestock industries in different countries (Bigras-Poulin et al., 2006; Bigras-Poulin et al., 2007; Natale et al., 2009; Lockhart et al., 2010; Volkova et al., 2010; Nöremark et al., 2011a; Rautureau et al., 2011; Rautureau et al., 2012b; Smith et al., 2012).

In Canada, there are limited studies describing network characteristics and contact pattern of swine herds . One study collected survey information about movement of swine and semen in Canada (Christensen et al., 2008). This study reported three types of farms: farms that had no movement at all (17%), farms with limited (<3) incoming movement but frequent outgoing movement (57%), and farms with frequent incoming and outgoing movement (26%) of animals during the 42 day study period. One recent study has used the network analysis approach to characterize movement of pigs between 251 swine farms of South-western Ontario and have demonstrated heterogeneity in

contact between production types, with nursery farms being central in the network (Dorjee et al., 2013).

In animal movement networks, farms are represented as nodes and the movement of animals between two farms is represented by a single link and the contact patterns among farms are evaluated using one-mode networks. In some instances, it is useful to evaluate the relationship between two distinct sets of entities (e.g. farms and trucks) and two-mode networks are used for this purpose (Borgatti and Everett, 1997). Previous studies related to the livestock sector have used two-mode networks to describe the relationship between farms and auction markets (Robinson and Christley, 2007), equipment and personnel sharing between cattle farms (Brennan et al., 2008), and truck sharing in the movement of pigs between French farms (Rautureau et al., 2012b) .

In addition to better understand the dynamics of infectious disease spread through the movement of animals, NA provides valuable information for the development of disease spread parameters in models to evaluate surveillance and disease control strategies. Failure to account for contact patterns among animal holdings in simulation models of disease spread will result in unrealistic model outcomes (Keeling and Eames, 2005b; Dubé et al., 2011b). In designing targeted surveillance programs for diseases associated with animal movements, herds selected based on their network parameters can enhance the sensitivity of the surveillance program (Dubé et al., 2011b; Frössling et al., 2012). Similarly, understanding network structures can guide the selection and improved targeting of control strategies to limit disease spread (Christley et al., 2005).

The objectives of this study were to describe farm to farm contact patterns of swine movement and the sharing of trucks used for those movements between swine farms in four Canadian regions using NA tools, as well as to obtain contact parameters for network-based simulation models for infectious disease spread in swine populations.

2.3 Materials and Methods

2.3.1 Swine movement data

Four months of swine movement data were obtained from a pilot pig traceability project conducted in four regions of Canada from July 1st to November 3rd, 2004. Regional pork boards selected the farms in each region that voluntarily agreed to participate in the study. The dataset included identification codes of shipping and receiving farms, date of shipment, number of animals shipped, production type, region and a unique identifier for the truck used in each shipment. A shipment was defined as movement of one or more pigs on the same day from a source to a destination farm. Each truck used for the shipment of pigs had a unique identifier and were used for single or multiple shipments during the study period. In case of multiple shipments by the same truck, it could be shared between different farms on the same day or on different days, or it could be pigs from multiple farms going to the same destination on the same day where pigs from different source farms shared the space during a particular shipment.

Descriptive summaries of the swine movement data, for the three time-scales considered in the study: overall (for the entire study period), monthly and weekly and for the four production types were computed in *Stata Statistical Software: Release 12* (StataCorp. 2011. College Station, TX, USA). The swine farms involved in this study comprised of

one of the four production types: farrowing farms that produced piglets which were delivered to nursery farms after weaning (at around 3 weeks of age), farrow to finish farms which produced marketable fattening pigs, nursery farms where pigs were reared after they were weaned but before fattening stage (approximately 3-10 weeks) and grower/finishing farms were mixture of farms rearing pigs either above 10 weeks to market age or after weaning till market age.

2.3.2 Network Analysis

One-mode and two-mode networks were constructed at the three different time scales: an overall network (for the entire study period), monthly (n=4) and weekly (n=18). There were 157 farms in the database that reported movement of pigs during the study period. Out of 157 farms, 12 farms were isolated, which either shipped animals to or received from farms outside the four study regions; these farms were not included in generation of one-mode networks. First, a series of farm to farm, directed, binary networks (one-mode) were generated to investigate the contact patterns between farms. In these networks, each unique farm was represented as a node and all the movements between two farms were consolidated as a single link. Then, to investigate the relationship between farms that shared trucks for the shipment of pigs, a farm to truck network (two-mode) was generated. In these two-mode networks (Borgatti and Everett, 1997), farms and trucks represented two sets of nodes and the sharing of trucks by farms was represented by links. For two-mode networks, the 12 isolated farms not included in the one-mode network were also included as the trucks they used for shipments were shared with other farms in the network. All network generation and analyses were performed using Ucinet (Version 6.414, Analytic Technologies, Harvard) .

The following network measures were computed for each network: size (number of nodes and links), degree (in and out-degree), density, fragmentation, average path length, and diameter. For the one-mode networks, the clustering coefficient and the reciprocity of links between nodes were also estimated. Two additional network measures, specific to one-mode networks, infection chain (in and outgoing) and components (strong and weak), were also computed and were used to compare the potential epidemic size of these networks. A description of network measures and other terminology relevant to this paper is presented in Table 2.1.

For the overall one-mode network the distributions of in-degree and out-degree, as well as ingoing and outgoing infection chains, were computed for each region and production type. ANOVA permutation tests, which do not rely on the assumption of independence of observation and random sampling (Borgatti et al., 2002),were performed to compare the distributions of in-degree, out-degree, ingoing and outgoing infection chains among production types in addition to the four regions . Correlation analyses were carried out using the Quadratic Assignment Procedure (QAP) to test whether farms had a higher degree of contact with farms of the same production type or within the same region. For QAP, first an attribute network based on the production type or region of the farms involved in an animal movement was generated and then its association with the overall one-mode network was tested with 10,000 permutations. QAP calculates Jaccard coefficient as a measure for similarity between two network matrices. Similarly, to assess whether ties between farms were associated with similarity in farm level network characteristics (in-degree, out-degree, number of trucks used by a farm) the Moran's *I*

autocorrelation coefficient was computed. Moran's *I* ranges from -1 to 1, with positive values representing positive autocorrelation.

To assess the presence of scale-free topology in the networks, a power-law distribution defined as $p(x) \sim x^{\alpha}$, was fitted to the observed in-degree and out-degree distributions of the monthly and overall one-mode networks and for degree (truck) distribution in the two-mode network. Degree distribution of weekly networks was not evaluated for presence of scale free topologies, as very few connections existed at that time scale. It is often difficult to estimate parameters for a power-law distribution, as in most cases only the tail of the observed distribution follows this distribution (Dubé et al., 2009). We used a maximum-likelihood estimator to estimate scaling parameter (alpha) and degree value (x) based on x_{min} (threshold value) and the Kolmogorov-Smirnov (KS) goodness-of-fit statistic to test power-law fit of the data as described by (Clauset et al., 2009). This analysis was conducted using the VGAM package (version 0.9-1 http://cran.r-project.org/web/packages/VGAM/index.html) in the R software platform with plfit.R, ConfidenceIntervals.R and GoodnessOf-Fit.R source code available at (http://tuvalu.santafe.edu/~aaronc/powerlaws/). Similarly, to ascertain small-world topology, 100 random networks with a similar number of nodes and links based on random graph theory (Erdős and Rényi, 1960) were generated using Ucinet (Version 6.414, Analytic Technologies, Harvard). Average clustering coefficients and average path lengths for the randomly generated networks were compared with each of the respective observed networks. A network was considered small-world, if the clustering coefficients were larger and the average path length was shorter than in the random networks of equivalent size.

Infection chain, components, out-degree (binary) based on a single link between two farms, and out-degree (valued) based on frequency of shipments between two farms which did not consolidated multiple shipments between pair of farms into a single link, were compared and evaluated for all three time scales to predict the potential size of an epidemic. Infection chains capture the number of links formed by animal movement between farms in the network and are defined by rules which are based on directionality of contact and time sequence of movement (Dubé et al., 2011a). These were extracted using the EpiContactTrace package (version 0.7.1 http://cran.r-project.org/web/packages/EpiContactTrace/index.html) available for the R software platform (R core team, 2012). The 95th percentile from the distribution of out-degree and outgoing infection chains and the sizes of the largest components, as well as giant strong component (GSC), were used to estimate the lower bound, while maximum values from the distribution of out-degree and outgoing infection chains as well as giant weak component (GWC) were used to estimate the upper bound of the potential epidemic size.

2.4 Results

2.4.1 Summary of swine movement

A summary of swine movement data from the four Canadian regions is presented in Table 2.2. The number of pigs moved on each day is shown in Figure 2.1. Weekly cycles of pig movement corresponding to weekdays can be noted. The number and percentage of animals moved and the number of incoming and outgoing shipments for each production type are presented in Table 2.3. The number and percentage of

shipments according to their origin and destination for each production type is presented in Table 2.4. Grower/finishing farms received the largest proportion of shipments (59.4%) with 45.8% of total animals received, followed by nursery farms (39.8% of shipments and 53.4% animals). Similarly, farrowing farms shipped the largest proportion of shipments and animals (35.6% and 39.5%), followed by grower/finishing farms (32% shipments and 26.2% animals) most of which were to farms of the same production type.

Out of 184 trucks used for the shipment of pigs, 29% of trucks were used in only a single shipment during the entire study period, while 25% of the trucks were used for 13 or more shipments. For more than 50% of the shipments on any particular day, the same truck was used for at least one other shipment and for approximately 10% of shipments the same truck shipped five or more shipments on a single day. When the same truck was used for two or more shipments on the same day, in 80% of the cases the truck carried multiple shipments, from different farms, at the same time.

2.4.2 One-mode networks

The one-mode overall network (Figure 2.2a) had 145 farms connected by 261 links. On the other hand, the monthly networks included 41-94% of all farms and around 27-89% of the number of links that existed in the overall network. As expected weekly networks involved a lower proportion of farms (1-60%) connected by only 0.4-33% of the total links present in the overall network. Summaries of these networks are presented in Table 2.5. The average number of connections per farm was 1.8 in the overall network and approximately one in the monthly and weekly networks. The number of farms with zero in-degree and zero out-degree in the overall network were 55 and 31, respectively.

Weekly networks presented a higher density (5%) as compared to monthly (0.5%) and overall networks (1.2%). The network showed a high degree of fragmentation at any time scale, indicating a high proportion of unreachable pairs of farms in the network. The fragmentation of the monthly and weekly networks was also evident from the number and size of their weak components. While the overall network had four weak components, the monthly and weekly networks presented 72 and eight weak components, respectively. The size of the largest weak component of each of these networks comprised 48%, 47% and 40% of the total farms in the respective networks.

The clustering coefficients of overall and monthly networks were larger than that of randomly generated networks (0.009 and 0.001 respectively) with similar number of nodes and links. However, clustering coefficients of weekly networks were of similar magnitude to that of randomly generated networks. Similarly, average path length of observed networks for all three time scales (1.8, 1.44 and 1.22) were shorter than that of randomly generated networks (6.75, 2 and 3.9 for overall, monthly and weekly networks).

There was not a single reciprocal link (Reciprocity=0) between farms in any of the one-mode networks, indicating that all of the shipments between farms were unidirectional. At all three time scales, any given pair of farms in the network was approximately two links apart and therefore could be reached through one intermediary farm. The longest path to reach any pair of farms (diameter) in the observed networks varied between 2 and 5 (Table 2.5). The size of the largest strong component for the overall, monthly and weekly networks was one, suggesting the absence of any subgroups of farms or any GSC within the networks.

The tails of the in-degree and out-degree distributions appeared linear on a log–log scale (Figures 2.3a/2.3b) with power-law exponent alpha values of 2.54 (95% CI 1.88-2.98) and 2.68 (95% CI 1.86-2.90), respectively, for farms with the highest in-degree (x_{min} >4) and out-degree (x_{min} >2) values. The KS test suggested that the power-law was a suitable distribution for both the in-degree and out-degree (p>= 0.68 and 0.22 respectively). Similarly, total degree (without considering directionality of movement) distribution also appeared linear on a log–log scale (Figure 2.3c) and had a power-law scaling exponent alpha value of 2.3 (95% CI 1.80-2.44) for farms with degree of more than four connections (x_{min}>4) and the KS test indicated this to be a plausible power-law distribution (p >= 0.17).

Based on permutation-based ANOVA tests, the distributions of in-degree, out-degree, ingoing and outgoing infection chains (Figure 2.4) were significantly different among production types (p<0.002), but not among regions (p>0.44). Nursery farms had higher in-degree and out-degree than other production types. They also had relatively large ingoing and outgoing infection chains. The in-degree and out-degree for nursery farms ranged from 1-7 (median: 3) and 0-6 (median: 2) respectively. Farrowing and farrow to finish farms had the lowest in-degree and ingoing infection chain values. Farrowing and farrow to finish farms had the highest outgoing infection chain and grower/finishing farms had highest ingoing infection chain. Farms in regions A and D (regions are not specified due to a confidentiality agreement) had higher in-degree and out-degree than farms in region B and D and farms in region A, B and D had higher in and outgoing infection chain than farms in region C, which corresponded to the fact that regions A and D had many nursery farms. However, none of these measures were significantly

different among the four regions. QAP analysis demonstrated that farms of the same production type were less likely to be linked with each other (Jaccard Coefficient=0.005, $p>0.95$), while farms within the same region were highly likely to be linked (Jaccard coefficient=0.67, $p<0.0001$). Similarly, farms tended to be connected with farms with similar out-degree (Moran's I=0.366, p<0.0001) but not with similar in-degree (Moran's I=0.08, p>=0.06). Links between farms were also associated with similarity in the number of trucks used by a farm (Moran's I=0.43, p<0.0001).

2.4.3 Two-mode network

The two-mode overall network (Figure 2.2b) contained 157 farms and 184 trucks. Similarly, the monthly and weekly networks involved 61% and 48% of farms and 47% and 27% of trucks respectively (Table 2.6). A farm used approximately five different trucks for shipments during the study period, while a truck was shared by approximately four farms. The overall two-mode network was less fragmented, compared to the one-mode network, indicating that including trucks in the network created additional paths and increased connectivity. The tail of degree distribution (for trucks) appeared linear on a log–log scale (Figure 2.3d) with a power-law exponent alpha value of 2.3 (95% CI 1.8-2.5), for trucks that were shared by more than three farms ($x_{min}>3$) and had a $p=0.15$ for the KS test, suggesting that the degree distribution of trucks followed a power-law distribution.

2.4.4 Comparison of potential epidemic size

A comparison among four network measures (out-degree (binary and valued), outgoing infection chain and component size) to estimate the lower (LB) and upper (UB) bound

of the potential epidemic size in one-mode networks at three different time scales is presented in Table 2.7. The components provided three times larger estimates than outgoing infection chain and approximately five to six times larger estimates than out-degree (binary) for UB of epidemic size in all three types of networks, however, estimates of component for lower bound were smallest of the three measures. The out-degree (binary) provided the smallest estimates for UB in all three networks, while out-degree (valued) provided larger estimates in terms of both UB and LB of epidemic size than outgoing infection chain.

2.5 **Discussion**

This study describes detailed contact structures among swine herds in Canada and explored the extent of truck sharing between farms. The swine industry in the regions studied was dynamically linked by animal movements; however the sharing of trucks also appears to be a significant source of inter farm connectivity. We studied the relationship between farms and farms that share trucks, by generating one-mode and two-mode networks at three different time scales.

This study included farms that voluntarily participated in the pilot traceability program and does not represent a random sample of farms in the four regions. The farms included in the study represented 5.6% of total swine farms in the four regions and ranged between 4-17% across the four regions (Statistics Canada, 2007). As the swine movement data used in this study were collected in 2004, there may have been some changes in frequency of shipments between farms. However, the pattern of swine movement and the topologies of the networks associated with swine movement are

likely to have remained largely unchanged particularly in terms of network topologies. This hypothesis is based on findings from studies of swine movement from Ontario, Canada (Dorjee et al., 2013) and from other European countries (Bigras-Poulin et al., 2007; Rautureau et al., 2012a; Büttner et al., 2013b) which suggests that swine movement networks in general demonstrate small-world and scale-free topologies. Network topologies has important implications in infectious disease spread and most network based disease simulation models utilize these network structures to simulate disease spread (Rahmandad and Sterman, 2008). Additionally, as other swine movement network studies have also suggested similar network measures as reported in this study, which is reflective of vertically integrated structure of the swine industry and trading relationship among swine operators which is much preferential and permanent (Dorjee et al., 2013{Smith, 2012 #64}{Nöremark, 2011 #74}), the farm level network measures (in-degree and out-degree) may still represent as reasonable estimates. However, due to voluntary participation of farms in the study, some bias in network level measures (fragmentation, density, clustering coefficient etc) may exist. Furthermore, this study included shipment activities of farms for only four months duration, thus any seasonal influence on the contact pattern between farms may not have been captured. Given the short duration of the study, voluntarily participation of the farms in the study and data assessed was not very current, generalizing and extrapolating some findings from this study will require some caution.

Ultimately, this study has highlighted the importance and necessity of recording movement data. Future studies in Canada with longer term movement data will provide additional insights on probable infectious disease spread via the movement of pigs and

will be able to identify any seasonal influences on such movements. Regulations in several European countries require reporting of animal movements and similar arrangements in Canada would not only aid in trace-back and trace-forward, but would also provide a rich database that could be explored to unravel a range of epidemiological questions.

The characteristics of the swine movement networks in these four regions of Canada were remarkably different from a network describing dairy cattle movement in Ontario (Dubé et al., 2011a). The swine movement networks were less fragmented, with larger clustering coefficients and degree values, but also with shorter path lengths. Moreover, a GSC was not observed in the swine movement networks, in contrast to the presence of a GSC, incorporating large subset of farms, reported in the network of dairy cattle (Dubé et al., 2011a). These differences reflects typical hierarchical production system of swine industry in which pigs at different stages of growth are raised in specific production facilities and movements of pigs between these facilities are unidirectional. However, some of the network measures (density, fragmentation and diameter) obtained in this study were similar to those described for a swine movement network in Southwestern Ontario, where both networks demonstrated similar topologies (Dorjee et al., 2013). It should be noted that the present study described movement of pigs in regions of Canada that excluded Ontario. Similarly, swine movement networks from other countries displayed comparable characteristics to those found here in terms of: degree distribution in a UK network (Smith et al., 2012); degree and infection chain distribution, density, and fragmentation in a Swedish network (Nöremark et al., 2011a); average path length in a French network (Rautureau et al., 2012b); and average path length and size of GSC

for the monthly network in a pork chain network in Northern Germany (Büttner et al., 2013c).

Several published animal movement networks (Lockhart et al., 2010; Dubé et al., 2011a; Rautureau et al., 2012b; Smith et al., 2012), present two basic patterns of connectivity, known as small world and scale-free topologies. Small world networks have higher local clustering than is the case for a random graph of the same size and are also connected with distant nodes by shorter paths (Watts and Strogatz, 1998). The overall and monthly (one-mode) networks in this study were characterized as having small-world topologies. However, the weekly networks topologies were similar to those found in random networks.

In scale-free networks, the frequency of contacts between nodes follows a power-law distribution, where many of the nodes have few connections while a few nodes have many connections (Barabási and Albert, 1999). It should be noted that small-world and scale-free topologies are not mutually exclusive and a network can exhibit both properties (Wang and Chen, 2003). In this study, the overall and monthly (one-mode) networks and the overall (two-mode) network were characterized as having scale-free topologies, as the in-degree and out-degree distributions of the one-mode networks and degree (truck) of the two-mode network fitted a power-law distribution, suggesting heterogeneity in the number of incoming and outgoing contacts for farms and in the sharing of trucks by farms.

Small-world and scale-free networks present two characteristically distinct topologies, when viewed from the perspective of disease spread and targeting surveillance and

control measures. In small-world networks, disease spread can occur quickly within clusters and can also reach distant farms in the network by crossing a few links, however the size of the epidemic in a small-world network tends to be smaller when compared to a random network (Christley et al., 2005). Due to the presence of hubs in scale-free networks, epidemics can spread faster than in random networks of similar size, but the spread of infection will gradually slow down once the primary (farms directly connected to hubs) and secondary contacts (farms not directly connected to hubs but connected to primary contacts)become infected (Kiss et al., 2006b; Kiss et al., 2006a). In terms of targeting control measures, scale-free networks are strong enough to withstand random attacks but are highly sensitive to targeted attacks (Nair and Vidal, 2011). Heterogeneity in degree distribution and the scale-free structure of a network indicates the presence of hubs (premises with high out-degree) and authority (premises with high in-degree). Hubs are central in disease spread and can be targeted to quickly reduce disease spread by applying control measures such as quarantine; similarly authorities can be central for targeting disease surveillance activities (Shirley and Rushton, 2005b; Martínez-López et al., 2009).

The high in- and out-degree as well as ingoing and outgoing infection chains associated with nursery farms represent their central position in receiving and spreading infection and suggest nursery farms could be potential target for disease surveillance as well as for applying control measures. The low in-degree and ingoing infection chain values associated with farrowing and farrow to finish farms indicate less vulnerability to acquiring infection from other farms via movement of animals. However, these farms had the highest risk of spreading an infection to other farms , as they have relatively

high out-degree and the highest outgoing infection chain values and targeting control measures at these farms could increase the efficiency of control program. Grower/finishing farms were likely to be the most vulnerable in terms of contracting an infection, based on their high in-degree and highest ingoing infection chain values. These findings are consistent with findings from other similar studies (Rautureau et al., 2012a; Büttner et al., 2013b; Dorjee et al., 2013) and can be explained by considering hierarchical structure of swine industry and unidirectional flow of pigs from one production type to other, where farrowing and farrow to finish farms are at the production end with high out-degree and outgoing infection chain values and finishing farms are at the receiving end with high in-degree and ingoing infection chain values (Büttner et al., 2013b).

Almost two thirds of the trucks used for shipment of pigs were shared between more than two farms. On any particular day, the same truck was shared between more than one farm in 50% of shipments, while on average each truck was shared by four different farms over the entire study period. Additionally, trucks increased the connectivity of farms in the swine movement network and decreased the number of links required to traverse the network from one farm to another. This could facilitate the spread of infectious agents to farms which would not be in direct contact otherwise. The truck itself can be considered as an epidemiological unit when it is contaminated.

Sharing of trucks potentially increases the risk of transmission of infectious agents in a number of ways: when animals from different farms share transport during shipment, or when animals from different farms are transported separately but in successive shipments, or through contamination of farm premises by infected fomites (Bigras-

Poulin et al., 2007). The role of shipment trucks in spreading PRRS virus to susceptible pigs has been documented (Dee et al., 2004b). Infected trucks may spread the disease unless they are cleaned and disinfected. Therefore, application of appropriate cleaning and disinfection protocols for shipment vehicles, as well as biosecurity measures at the farm gate may be crucial in limiting the spread of diseases via shared trucks (Dee et al., 2004a). However, a recent study in Canada reported that less than one third of trucks used for the shipment of pigs are cleaned and disinfected between successive shipments (Lambert et al., 2012b) suggesting that regular cleaning and disinfection of shipment vehicles is not an usual practice. This may have serious implications in facilitating the spread of disease in networks such as those described in this study.

Understanding the characteristics of swine movement networks in Canada, combined with knowledge of indirect contacts between swine farms via the sharing of trucks may be useful to producers when evaluating existing biosecurity plans, to professional organizations in developing biosecurity guidelines, and to policy makers in developing control strategies for emerging diseases.

The outgoing infection chain measure is likely the best estimator of potential epidemic size in networks for all time scales, rather than out-degree or size of the largest components. Similar predictions were reported from a study of swine movement network in Northern Germany (Büttner et al., 2013c). The fact that the infection chain represents the directed path of animal movement across farms by taking the actual time sequence of movements into account (Dubé et al., 2008) increases the reliability of this measure in predicting epidemic size. Our findings suggest that the introduction of a pathogen of short incubation period into the network could infect up to six farms (in the

weekly network) and if the infection remained undetected for four months then up to 20 farms could become infected (14% of the total farms in the network).

The out-degree (binary) tended to predict smaller potential epidemic size; this is not surprising, as out-degree only accounts for immediate contacts and does not consider any subsequent contact beyond primary contact. However, out-degree (valued), which is based on the frequency of outgoing shipments from a farm and does not consolidate multiple shipments to the same farm into a single link, estimated larger epidemic sizes than did the outgoing infection chain. This finding suggests that using frequency of shipments to estimate contact rates between farms, as an input parameter for disease spread models, will eventually predict larger epidemic sizes.

Similarly, GSC and GWC predicted the smaller, lower bound and larger upper bound of potential epidemic size when compared to estimates based on the infection chain. Neither GSC nor GWC account for the time sequence of shipments, nor does the GWC account for direction of movements. The potential epidemic size estimated in this study was based on direct contact between farms (movement of animals) and did not consider any other routes of transmission, such as indirect contacts (sharing of trucks, personnel, equipments etc.), transmission by vectors or aerosol spread. Additionally, the biosecurity level of the farms was not considered as well, which could strongly influence the estimated potential epidemic size.

This study provided some of the contact parameters required to simulate the spread of infectious diseases between swine farms. First, it identified the network structure as small-world and scale-free. This information can be used in defining the network and

the associated topology. Second, contact frequency and out-degree between different pairs of production types can be used to define the contact rates between farms in simulation models. In addition, the degree distribution of trucks can be used to parameterize indirect contacts by truck sharing in network based models.

2.6. Conclusion

This study has provided novel insights into the contact pattern among swine herds in four Canadian regions. As expected, the swine movement networks described demonstrate a production system with a hierarchical structure and heterogeneities in contact levels between farms. The findings also indicated that many farms that would otherwise not be linked were connected indirectly via the sharing of trucks used for pig shipments. Understanding the structure of swine movement networks should assist in providing advice on targeted surveillance as well as in the control of infectious diseases such as PRRS. This knowledge should also encourage the proper cleaning and disinfection of shipment vehicles between successive shipments, which will decrease the number of potentially infective contacts between farms. Finally, contact parameters from this swine movement network can be used to represent heterogeneity in contacts between farms in simulation studies of infectious disease spread in Canadian swine populations.

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Table 2.1 Description of network analysis terminology as used in the context of animal movement networks

(Based on material discussed in: Borgatti and Everett, 1997; Watts and Strogatz, 1998; Dubé et al., 2009; Opsahl and Panzarasa, 2009)

Term	Definition
Node	The unit of interest (farms) in the network
Arc	A directed link between two farms
Binary network	When multiple links (shipments in this study) between two specific farms are considered as a single link (occurred / did-not-occur)
Valued network	When frequency or value of links between two specific farms are taken into account
One-mode network	A network with one set of nodes (farm to farm network)
Two-mode network	A network with two distinct sets of nodes (farm to truck, farm to market networks)
Density	Proportion of actual links present in the network over all possible links
Degree (one-mode)	
In-degree	Number of farms from which each farm receives animals
Out-degree	Number of farms to which each farm sends animals
Degree (two-mode)	
Degree (farm)	Number of trucks used by that farm for shipments
Degree (truck)	Number of farms sharing that truck for shipment
Strong component	Maximally connected subgroup of a network where all farms are directly linked
Weak component	Maximally connected subgroup of a network without considering directionality of the links
Clustering Coefficient (one-mode)	The proportion of closed triplets (formed by 3 farms connected by 3 undirected links) to total number of open (formed by 3 farms connected by 2 undirected links) and closed triplets in the network
Average Path Length	The average number of links along the shortest or geodesic paths between all possible pairs of nodes
Diameter	Longest path between any pair of farms in the network
Fragmentation	Proportion of pair of farms that are unreachable in the network
Reciprocity	Proportion of reciprocated links in the network
Ingoing Infection Chain	Number of direct and indirect incoming contacts to a farm through other farms by incorporating sequence of contacts
Outgoing Infection Chain	Number of direct and indirect outgoing contacts from a farm through other farms by incorporating sequence of contacts
Small-world Network	A network with high clustering and short path length compared to a randomly generated network with same number of nodes and links.
Scale-free network	A network with heterogeneity in degree distribution, where degree distribution fits a power-law distribution (many farms have few connections and a few farms have many connections)

Table 2.2 Summary of swine movement data in four Canadian regions from July to November 2004

Description	Overall value	Monthly Shipment Mean (Min-Max)	Weekly shipment Mean (Min-Max)
Number of Farms	157	99 (73-122)	67 (8-95)
Number of Shipments	2043	511 (307-727)	72 (6-113)
Number of trucks used for shipments	184	85 (54-113)	44 (3-65)
Average number of shipments/truck (Range)	11 (1-163)	6 (5-7)	1.6 (1.45-2)
Mean Shipment Size (Range)	130.5 (1-700)	125.2 (111-143)	78.2 (54.6-160.7)
Average number of shipments/ farm (Range)	14.7 (1-48)	6.1 (4.8-7.3)	1.5 (1.2-1.7)
Days of activity	106 (July 1-Nov 3, 2004)	26.5 (24-28)	5.9 (4-7)

Table 2.3 Number of swine shipments and number of pigs moved by production type in four Canadian regions from July to November of 2004

Farm Type	No. of farms (%)	Incoming shipment		Outgoing shipment	
		Shipments	Animals (%)	Shipments	Animals (%)
Grower/finishing	78 (49.7)	934	59,108 (45.8)	503	56,387 (28.6)
Farrowing	32 (20.4)	12	1,104 (0.8)	559	85,008(43.1)
Farrow to finish	11 (7)	0	0	273	41,348 (21.0)
Nursery	36 (22.9)	626	68,801(53.4)	237	14,288 (7.3)
Total	157	1572	129,013	1572	197031

Table 2.4 Total number of swine shipments by production type of source and destination farms, in four Canadian regions from July to November of 2004

Source farm	Destination farm				
	Grower/finishing	Farrowing	Farrow to finish	Nursery	Total (%)
Grower/finishing	477	-	-	26	503 (32.0)
Farrowing	35	12	-	512	559 (35.6)
Farrow to finish	204	-	-	69	273 (17.4)
Nursery	218	-	-	19	237 (15.1)
Total (%)	934 (59.4)	12 (0.8)	-	626 (39.8)	1572

Table 2.5 Descriptive network measures for one-mode binary networks (overall, monthly and weekly) of swine movement in four Canadian regions from July to November of 2004

Network Measures	Overall Network	Monthly Networks Mean (Range)	Weekly Networks Mean (Range)
Size	145	92 (59-137)	52 (2-87)
Links	261	131 (71-232)	50 (1-86)
Average Degree	1.8	1.36 (1.20-1.70)	0.90(0.50-1.10)
Median In-degree (range)	1(0-26)	0.5 (0-24)	0 (0-17)
Median Out-degree (range)	1(0-10)	1 (0-8)	0 (0-5)
Density	0.012	0.005 (0.003-0.009)	0.050 (0.01-0.500)
Clustering Coefficient	0.06	0.03 (0.02-0.05)	0.02 (0.00-0.04)
Av. Path Length	1.80	1.44 (1.38-1.57)	1.22 (1.02-1.57)
Diameter	5	3.25 (3-4)	2.5 (2-3)
Fragmentation	0.98	0.99 (0.98 - 0.99)	0.96 (087-0.99)
Reciprocity	0	0	0
Weak Component			
Number	4	72 (26-105)	8 (5-15)
Largest Size	69	43 (28-69)	21 (10-31)
Strong Component			
Number	145	92 (59-137)	57 (2-87)
Largest Size	1	1 (1-1)	1 (1-1)
Outgoing Infection Chain			
Mean/ Range	3 (0-20)	1.86 (0-17)	1.30 (0-6)
Ingoing Infection Chain			
Mean/ Range	3 (0-40)	1.86 (0-34)	1.30 (0-23)

Table 2.6 Descriptive network measures for the two-mode networks (overall, monthly and weekly) of swine movement in four Canadian regions from July to November of 2004

Network Measures	Overall Network	Monthly Network Mean (Range)	Weekly Networks Mean (Range)
Size			
Farms	157	96 (73-114)	75 (33-97)
Trucks	184	86 (55-114)	49 (19-67)
Links	717	273 (174-368)	137 (49-183)
Average Degree (Range)			
Farms	4.56 (1-39)	2.76 (2.22-3.30)	1.79 (1.48-1.88)
Trucks	3.90 (2-22)	3.1 (2.70-3.50)	2.76 (2.38-3.10)
Density	0.025	0.012 (0.007-0.014)	0.004 (0.002-0.006)
Average Path Length	4.31	4.45 (4.0-5.0)	3.31 (1.45-4.1)
Diameter	12	12 (9-14)	9 (2-13)
Fragmentation	0.55	0.88 (0.81-0.95)	0.94 (0.89-0.98)

Table 2.7 Number of nodes (farms) determined by the lower and upper bounds of four network measures obtained from the swine movement information from four Canadian regions from July to November of 2004.

Network measures	Overall Network		Monthly Networks		Weekly Networks	
	LB	UB	LB	UB	LB	UB
Out-degree (binary)[a]	5	10	5	8	4	5
Out-degree (valued)[a]	32	52	10	16	5	8
Outgoing infection chain[a]	12	20	8	17	4	6
Component[b]	1	69	1	43	1	21

[a]LB and UB are 95th percentile and maximum value from the distribution
[b]LB and UB are sizes of the largest strong and weak components, respectively.

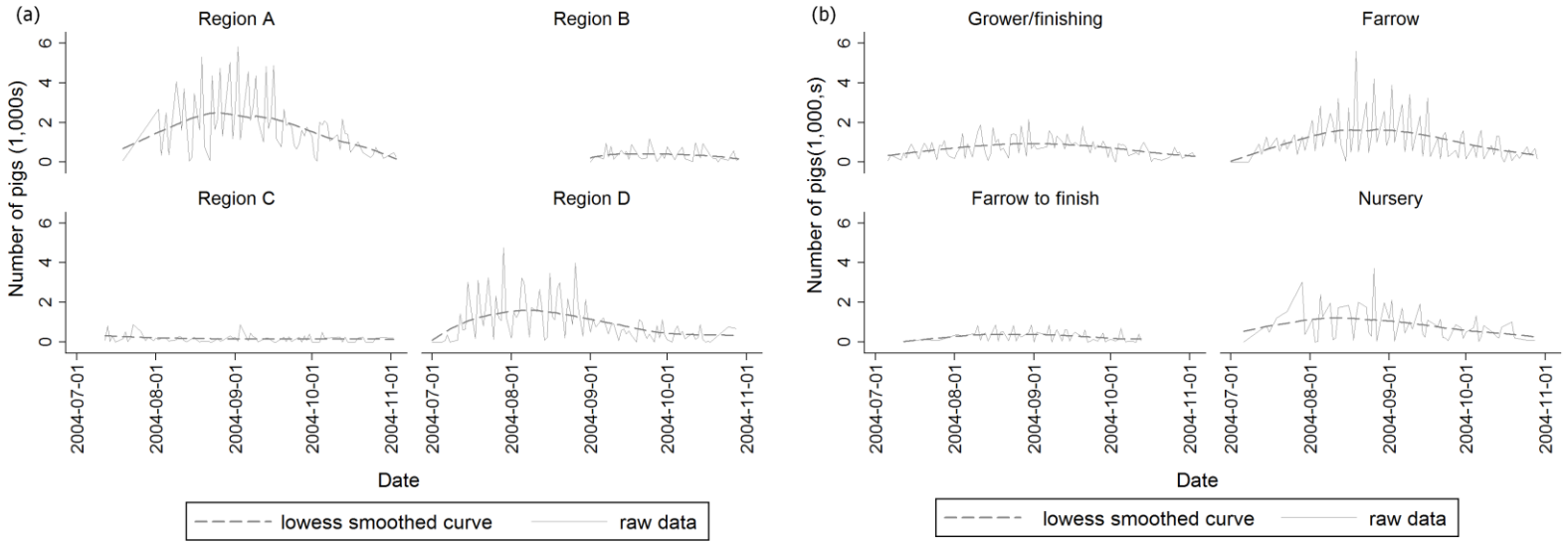

Figure 2.1 Daily movement of pigs from 1 July 2004 to 3 November 2004 in four Canadian regions with lowess smothing (bandwidth 0.8) by region (a), and production type (b).

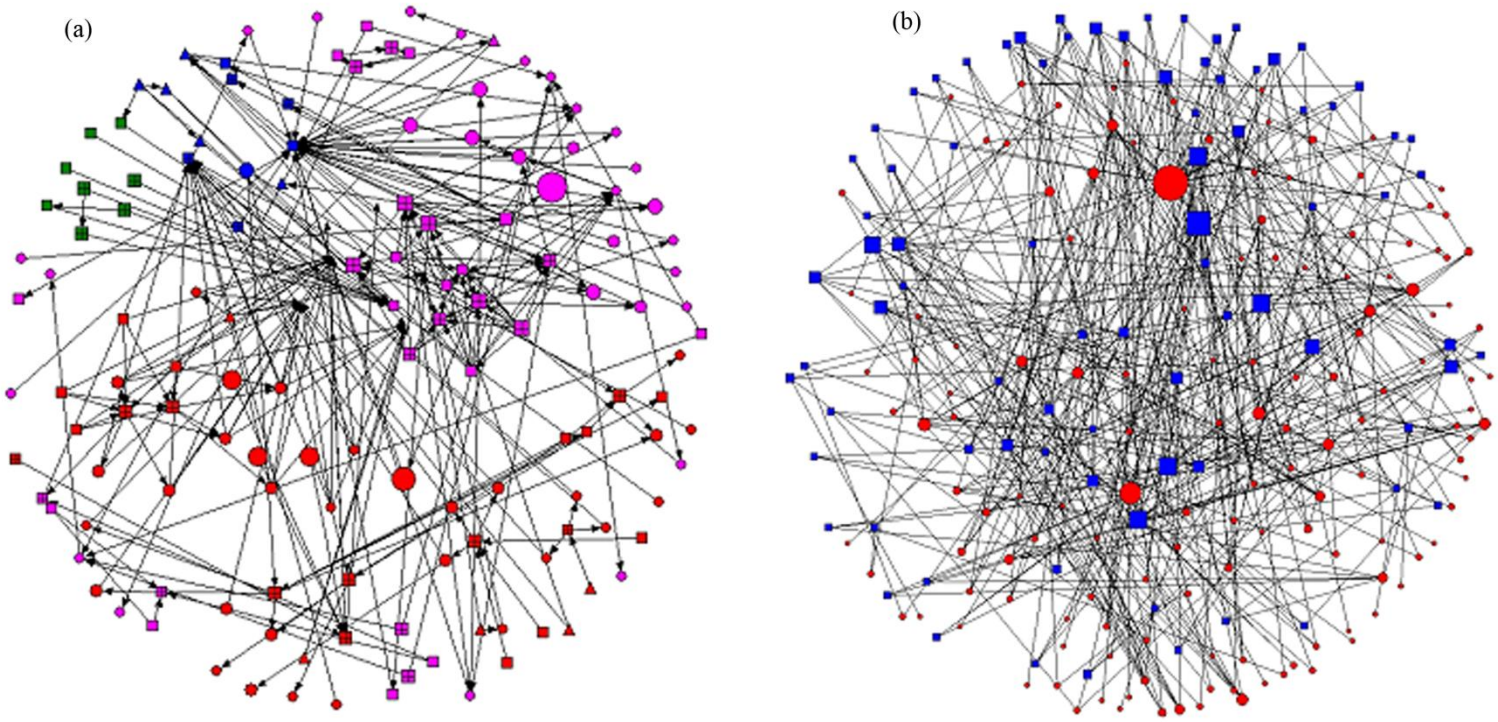

Figure 2.2 (a) One-mode network diagram of pig movements in four Canadian regions (N=145) Node color indicates regions (Red: A, Blue B, Green: C, and Pink: D) and node shape indicates farm type (circle: grower/finishing, square: farrowing, up triangle: farrow to finish, and box: nursery). The largest circles represent farms with largest outgoing infection chain values. (b) Two-mode network map of pig movements in four Canadian regions from July 1st to November 3rd of 2004, N1 (Farms=157, represented by red circles) and N2 (Trucks=184, represented by blue squares). The size of each node is proportional to the degree centrality of that entity.

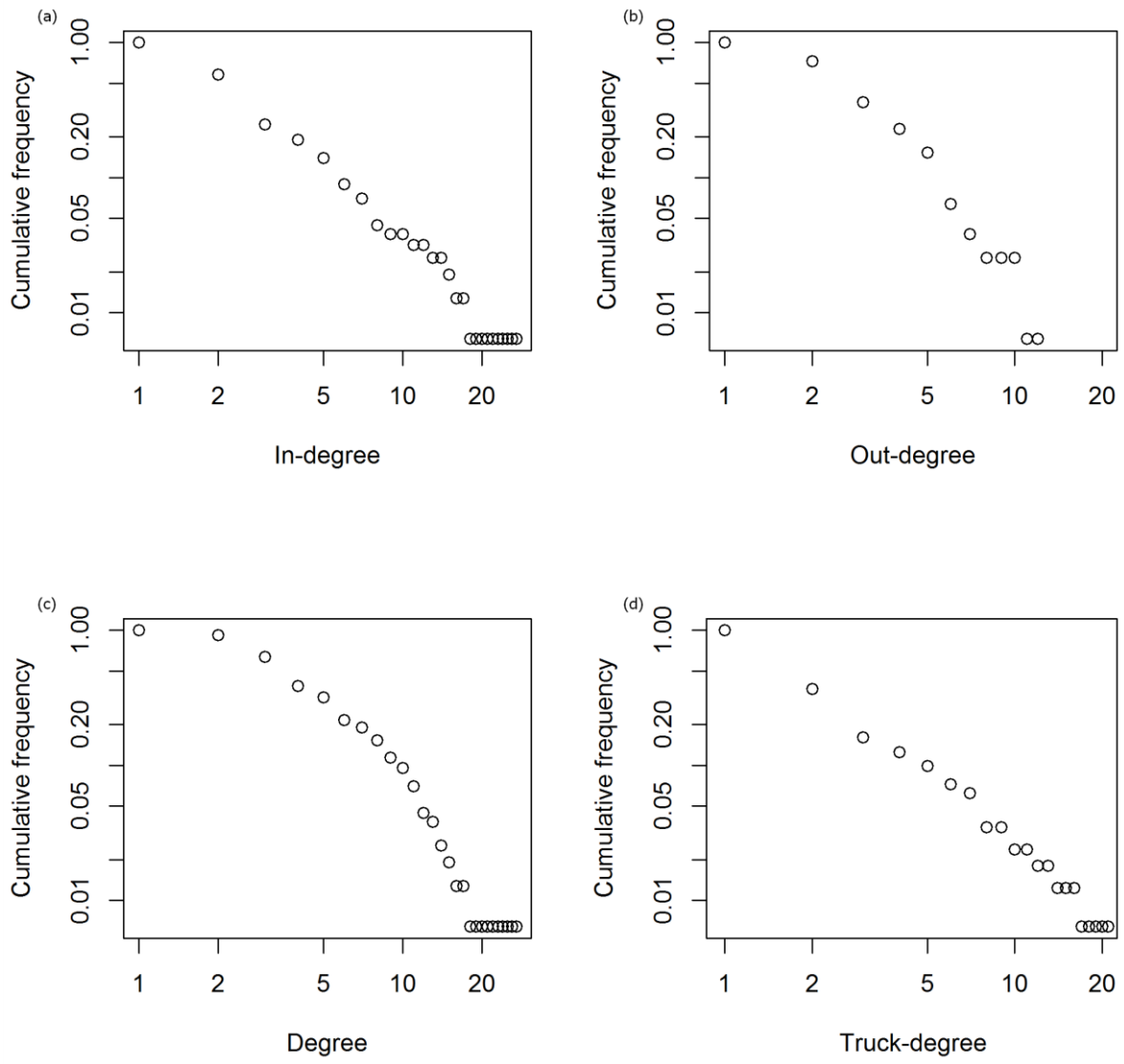

Figure 2.3 (a-c) Distribution of in-degree, out-degree and total degree of farms in the one-mode overall network and (d) degree of truck in the two-mode network of swine movements in four Canadian regions from 1 July to 3 November 2004.

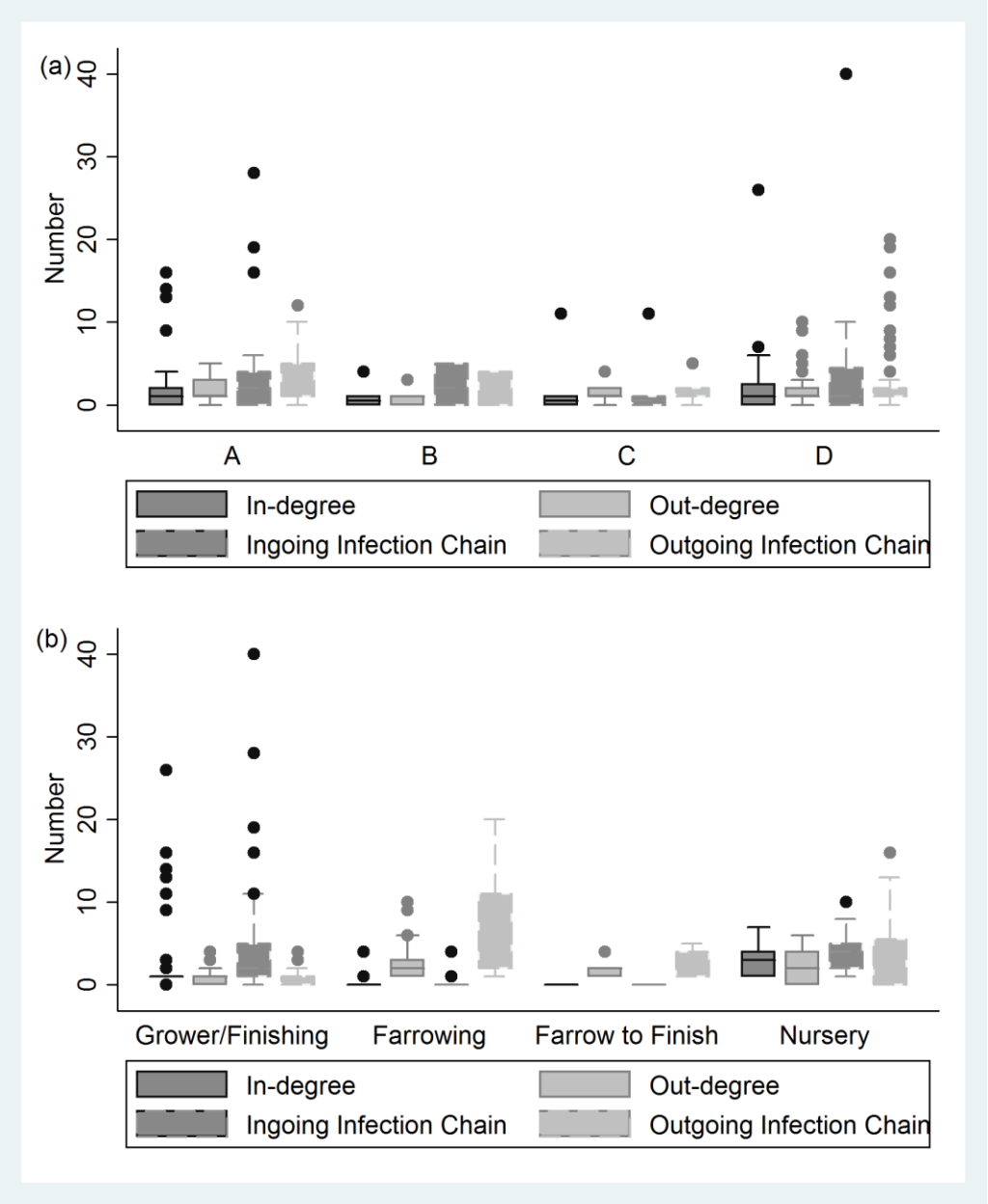

Figure 2.4 Distribution of in-degree, out-degree, ingoing and outgoing infection chain of farms in the one-mode overall network of swine movements in four Canadian regions from 1 July 3 November 2004, by region (a), and by production type (b).

Chapter 3 Simulation of between-farm transmission of porcine reproductive and respiratory syndrome virus in Ontario, Canada using the North American Animal Disease Spread Model

The contents of this chapter are published as, Thakur K, Hurnik D, Poljak Z, Revie C, Sanchez J. (2015), Simulation of between farm transmission of porcine reproductive and respiratory syndrome virus in Ontario, Canada using North American Animal Disease Spread Model. Preventive Veterinary Medicine, DOI: 10.1016/j.prevetmed.2015.01.006

3.1 Abstract

Porcine reproductive and respiratory syndrome (PRRS), a viral disease of swine, has major economic impacts on the swine industry. The North American Animal Disease Spread Model (NAADSM) is a spatial, stochastic, farm level state-transition modeling framework originally developed to simulate highly contagious and foreign livestock diseases. The objectives of this study were to develop a model to simulate between-farm spread of a homologous strain of PRRS virus in Ontario swine farms via direct (animal movement) and indirect (sharing of trucks between farms) contacts using the NAADSM and to compare the patterns and extent of outbreak under different simulated conditions. A total of 2552 swine farms in Ontario province were allocated to each census division of Ontario and geo-locations of the farms were randomly generated within the agriculture land of each Census Division. Contact rates among different production types were obtained using pig movement information from four regions in Canada. A total of 24 scenarios were developed involving various direct (movement of infected animals) and indirect (pig transportation trucks) contact parameters in combination with alternating the production type of the farm in which the infection was seeded. Outbreaks were simulated for one year with 1000 replications. The median number of farms infected, proportion of farms with multiple outbreaks and time to reach the peak epidemic were used to compare the size, progression and extent of outbreaks. Scenarios involving spread only by direct contact between farms resulted in outbreaks where the median percentage of infected farms ranged from 31.5 to 37% of all farms. In scenarios with both direct and indirect contact, the median percentage of infected farms increased to a range from 41.6 to 48.6%. Furthermore, scenarios with both direct and indirect contact resulted in a 44% increase in median epidemic size when compared to the direct

contact scenarios. Incorporation of both animal movements and the sharing of trucks within the model indicated that the effect of direct and indirect contact may be nonlinear on outbreak progression. The increase of 44% in epidemic size when indirect contact, via sharing of trucks, was incorporated into the model highlights the importance of proper biosecurity measures in preventing transmission of the PRRS virus. Simulation of between-farm spread of the PRRS virus in swine farms has highlighted the relative importance of direct and indirect contact and provides important insights regarding the possible patterns and extent of spread of the PRRS virus in a completely susceptible population with herd demographics similar to those found in Ontario, Canada.

3.2. Introduction

Porcine reproductive and respiratory syndrome (PRRS) is an important viral disease of swine and has major economic impacts on the swine industry (Neumann et al., 2005). PRRS affects all production stages and is characterised by late-term abortions, still-births, mummified foetuses and weak piglets in breeding herds; and an increased mortality rate in piglets and respiratory disease, poor growth performance and mortality in growing pigs (Nodelijk, 2002). The causative agent for PRRS is an enveloped, spherical, single stranded, positive-sense RNA virus of the family Arteriviridae (Murtaugh et al., 1995). Genetic studies of the virus indicate significant antigenic and molecular variability, suggesting two distinct genotypes: Type I (European genotype) and Type II (North American genotype). Wide genotypic variation within each genotype is another notable characteristic of this virus (Murtaugh et al., 1998).

The virus is present in serum and excreted in several bodily secretions, which include semen, colostrum, urine, feces and oral fluids of infected animals (Wills et al., 1997c;

Bierk et al., 2001). Survival of the PRRS virus in the environment is affected by ambient temperature and pH. The virus can survive for long periods (four months) at temperatures below -20^{0}C; however, at higher temperatures viability of the virus decreases. It can remain infective for around one month at 4^{0}C, six days at 21^{0}C, one day at 37^{0}C, and for only 20 minutes at 56^{0}C (Benfield et al., 1992).

Several mechanisms for transmission of the virus between farms have been outlined; the most important and widely agreed upon mechanisms are via the movement of infected animals between different farms / stages of swine production, and through the introduction of infected semen (Yaeger et al., 1993; Mortensen et al., 2002). Vehicles used for the transportation of pigs and associated fomites (boots, coveralls, bedding materials etc) can also spread the infection over long geographical distances, as has been demonstrated in a number of transmission experiments using contaminated vehicles and fomites (Dee et al., 2002a; Otake et al., 2002c; Dee et al., 2004b; Holtkamp et al., 2010). Local transmission by aerosols within 150 metres has also been reported from an experimental study (Otake et al., 2002a).

Simulation models which explore artificially designed experiments have become an important tool for epidemiologists to simulate the spread of a range of infectious diseases of livestock (Kao, 2002; Kobayashi et al., 2007; Evans et al., 2010). Such ‘experiments’ would not normally be possible in real world conditions, due to cost, time and/or animal welfare considerations. Disease spread models are intended to mimic real world situations and can be useful in explaining the behaviour of complex biological systems; identifying the key factors influencing a system, predicting the effect of interventions on disease outcomes and providing a means to inform policy decisions

(Taylor and Gate, 2003). NAADSM (North American Animal Disease Spread Model) is a spatial, stochastic, farm level state-transition modeling framework originally developed to simulate the between-farm spread of highly contagious and foreign livestock diseases (Harvey et al., 2007). It allows for user-established parameters to define model behaviour in terms of disease progression, has flexibility to simulate disease spread by direct contact through the movement of animals, indirect contact via personnel or fomites, airborne dissemination and local spread. In NAADSM the individual population units (farms) are defined by their actual physical location within a geographical region. The disease spread between individual farms in NAADSM is influenced by rates of direct and indirect contact, relative locations and distances between farms; all of which are driven by stochastic processes based on distributions and relational functions specified by the user. Once a farm has become infected it follows a natural, predictable cycle over time, transiting from one to another disease state (Harvey et al., 2007). One key advantage of this approach is that by including randomness, the chance nature of epidemic spread is accounted for, while by incorporating the contact structure between farms a higher degree of realism can be achieved in the model (Dangerfield et al., 2009).

A single study, so far, has been published which attempt to evaluate the between-farm transmission dynamics of PRRS virus and outline the extent of disease spread in a geographical region. Neumann et al. (2007) evaluated the risk of introduction of the PRRS virus into New Zealand through the importation of raw pig meat and predicted the extent of any subsequent spread of the virus within the swine industry in New Zealand. Additionally, truck sharing between farms for shipment of pigs has been considered to

be one of the major pathways for between-farm spread of PRRS virus by Canadian producers (http://www.opic.on.ca/biosecurity-resources/transportation) and experts in the swine industry. Recent studies have demonstrated high levels of truck sharing between farms for the shipment of pigs (Bottoms et al., 2012b; Thakur et al., 2014) and have documented that only around one third of such trucks are properly cleaned and disinfected between successive shipments (Lambert et al., 2012b). However, the likely impact of truck sharing on the spread of PRRS virus has not been explored in previous studies. So, this study attempted to describe the likely spread of PRRS virus due to movement of pigs between farms and indirect contact associated with such movement. The objectives of this study were to develop a model to simulate the between-farm spread of PRRS virus in Ontario swine farms via direct (animal movement) and indirect (sharing of trucks between farms) contacts using the NAADSM framework and to describe and compare the patterns of outbreak under a range of scenarios.

3.3. Materials and Methods

3.3.1 Study population

As NAADSM simulates the spread of a pathogen between farms, it requires the geographical location of each farm together with its characteristics (herd size and production type). For reasons of confidentiality, the actual geographical coordinates of swine farms in Ontario and other farm attributes were not available. We therefore generated hypothetical geographical locations to represent swine farms in Ontario. Data on the total number of swine farms in Ontario and on numbers of swine farms in each Census Division (CD) of Ontario province were downloaded from Statistics Canada website (Farm and Farm Operator Data, 2011). Using the Agricultural and Ontario

shape files, a range of random points corresponding to the number of farms in each census division of Ontario were generated using QGIS (Quantum GIS development Team 2012. QGIS version number 1.8.0); the longitude and latitude of these points were extracted and used as farm locations in NAADSM. The randomly generated farm locations were constrained to be within agricultural parcels and were at least 500 meter apart from one another. According to the 2011 agriculture census report, Ontario had a total of 2556 swine farms; however, our study included only 2552 swine farms as four of the randomly generated farms were located in census divisions that had no agricultural land. The density of swine farms in each census division of Ontario, and the spatial distribution of modelled farms by production type, is shown in Figures 3.1 a and b, respectively. To evaluate the effect of artificial geolocations of farms on simulated outcomes, three different sets of farm locations were created on which PRRS virus spread was simulated for comparison.

These 2552 farms were randomly assigned to one of six production types: farrowing, nurseryA, finishingA, farrow-to-finish, nurseryC and finishingC (Table 3.1); the random assignment of production types was reasonable as, based on experts' judgement, farms of a particular production type are not spatially clustered in Ontario. The proportion distributed to each of the broad production types was based on a previous pig traceability study (Thakur et al., 2014) or based on experts' judgement, in the case of farrow-to-finish farms. In addition, 60% of nursery and finishing farms were classified as having adopted the practice of all-in-all-out (AIAO, farm types given the suffix "A") with the remaining 40% adopted the continuous flow (CF, farm types with suffix "C")

approach. This division was based on experts' judgement regarding the average distribution of farms practicing AIAO versus CF practices in Ontario.

In NAADSM, herd size has two implications on disease progression. First, the size of source farms may influence infectiousness of the herd, as conceptually larger farms could have more infectious animals expelling the virus and then increasing the probability of disease transmission. However, we considered the whole farm to be infectious once a single animal on the farm was infected and the transmission probability was independent of herd size. Second, NAADSM assigns higher probability of receiving a contact for larger farms within the same distance distribution than for smaller farms. However, in a vertically integrated commercial system, such as swine production in Ontario, the probability of contact between farms due to movements of pigs is less likely to be associated with the herd size of a recipient farm. For farms within the same distance, in NAADSM, larger farms are more likely to receive the contact which in our model should be a random process given that all the farms within the contact group are equally likely to have contact with other farms in that contact group, irrespective of farm size. Therefore, to avoid any influence of farm size in assigning the contacts, as NAADSM prefers sending shipments to larger farms, the following assumptions were made. Each swine farm was assigned 500 pigs per farm and it remained fixed for the entire duration of simulation.

3.3.2 Model Structure

To determine the pattern and extent of spread of PRRS virus from infected to susceptible farms in Ontario, Canada, a spatially explicit, stochastic, farm-level state-transition computer simulation was developed using NAADSM (*NAADSM*

Development Team 2011. *NAADSM* version number 4.0). One farm was randomly chosen to be seeded with an infection and the same farm initiated infection in subsequent iterations. The rest of the farms were susceptible at the beginning of the simulation and after being infected they either remained infectious (for farrowing, farrow-to-finish, nurseryC and finishingC farms) until the end of the simulation or became susceptible, following the SIS state transition approach (for nurseryA and finishingA farms). Change in state of any nurseryA and finishingA farm on any time-step during the model run was determined stochastically based on random sampling from the infectious duration distributions specified in the model.

3.3.3 Model Outcomes

The spread of PRRS virus in the population was initiated by setting an index farm as being infected. Each scenario was simulated on a weekly time scale for up to 52 weeks and was replicated for 1000 iterations (representing 1000 independent *in-silico* outbreaks). Median final epidemic size, median number of total farms infected, and time to peak epidemic were computed for each scenario. Final epidemic size was defined as the total number of outbreaks at the end of each iteration, irrespective of whether a farm remained infectious at the end of the simulation period and also counted multiple outbreaks in the same farm. Since pigs in nurseryA and finishingA farms stay for a shorter duration compared with animals from continuous flow farms, such farms could have multiple outbreaks over the duration of the simulation. It was for this reason that it was important to capture the final epidemic size in addition to the number of infected farms, so that multiple outbreaks on the same farm would count towards an increase in overall epidemic size. For median number of farms infected, farms that had multiple

infections were counted only once; while for median epidemic size, farms with multiple outbreaks were counted multiple times. Additionally, we extracted the percentage of farms of each production type with and without any infection and the percentage of nurseryA and finishingA farms that had experienced multiple outbreaks during each simulation. The time to peak epidemic was defined as the number of weeks taken to reach the epidemic peak, where epidemic peak was defined as the maximum number of infected farms in any one time unit across the simulation.

3.3.4 Assumptions

Though PRRS virus is currently circulating in swine farms in Ontario, in this study we assumed that all farms in this study were free of PRRS at the beginning of the simulation and this can be a case when a new strain of virus is introduced where there is no immunity to the new strain. We further assumed that a homologous strain of PRRS virus was seeded for initiation of the outbreak and the virus did not mutate during the course of the simulation. When a single animal on a farm became infected the entire farm was considered infectious. Furthermore, we assumed that in any outgoing shipment from an infectious farm at least one infected animal would be present in the shipment which is equivalent to having a probability of 1 for transmission of the virus when a shipment occurs from an infected farm. Every farm had the same probability to contact other farms given the distance between source and recipient farms and the pre-defined production type combinations. Lastly, for indirect contact we used the sharing of the same transportation vehicles between farms for shipment of incoming or outgoing animals. However, when two farms already had direct contact, the sharing of trucks implicit in such a contact was not counted again as part of the indirect contact.

Additionally, we did not consider any other forms of indirect contact, such as the movement of personnel or the sharing of equipment. As we wished to evaluate the impact of a worst case scenario with respect to the cleaning of trucks on spread of the virus, we assumed that trucks used for shipment of animals were "dirty trucks", as would be the case if the trucks were not properly cleaned and disinfected between successive shipments. For indirect contact, the transmission probability was assumed to be very low (0.1), compared to the direct contact transmission probability (1).

3.3.5 Parameters

Many parameters relating to PRRS virus transmission were extracted from the published literature (Lager et al., 1997; Neumann et al., 2007; Evans et al., 2010). To simulate spread by direct and indirect contact, contact parameters were derived from swine movement data collected as part of a pilot study in four Canadian regions (Thakur et al., 2014). Two co-authors of this manuscript (DH, a Professor of swine health management, and ZP, an Associate Professor of Veterinary Epidemiology whose research has a focus on swine disease), have extensive expertise in swine production and management across Canada and provided inputs to establish the model structure. They also provided estimates for a number of parameters (infectious duration and direct contact rate for nurseryA and finishingA farms, distance distribution for recipient units and proportion of AIAO and continuous flow farms) that were not available in the published literature and could not be estimated from the pilot study data. Direct contact was defined as the movement of at least one pig from one farm to another. Indirect contact in this model specifically included contacts between farms that occurred as a result of sharing of the same transport vehicles (e.g. shipment of animals) within the

period of one week (one time-step of the model). This time period was chosen, as the virus remains infective for around a week at 21^0C.

NAADSM requires three parameters to simulate a contact: the mean contact rate (expected number of contacts per week); the transmission probability associated with that contact; and the geographical distance distribution associated with contact between any two farms (Harvey et al., 2007). For between-farm transmission of the PRRS virus by direct contact, we used a fixed transmission probability (i.e. 1), as was used in a model of this disease in New Zealand (Neumann et al., 2007). For probability of transmission via indirect contact, we assigned a lower value (0.1), which was based on our assumptions; and we evaluated the impact of this assumption on modelled outcomes by carrying out a sensitivity analysis across a range of transmission probabilities. PRRS virus persists for an extended period of time in the tissues of infected animals (Nodelijk et al., 2000). In addition, PRRS virus infected farms (farrowing, farrow-to-finish, nurseryC and finishingC) can remain infectious for long periods of time (Nodelijk et al., 2003) as new susceptible animals are continuously replaced throughout the production period. Therefore, we assumed an infectious period of one year for these farms, following the SI (Susceptible-Infectious) state transition approach (Keeling and Rohani, 2008), as reported by Neumann et al., (2007). On the other hand, nurseryA and finishingA farms were assumed to adopt an AIAO production system, so these farms followed the SIS (Susceptible-Infectious -Susceptible) state transition approach (Keeling and Rohani, 2008) and the infectious period for these farms was tied to their production cycle. With the turnout of each batch of pigs these farms are assumed to get rid of any

infection, by allowing a downtime period of two weeks between successive batches for proper cleaning and disinfection procedures.

The mean contact rate, as required by NAADSM, was used as the parameter of a Poisson distribution. This mean was estimated for both direct and indirect contacts as follows: we first generated a valued contact matrix of frequency of contact among each of the production types using the swine movement data. Subsequently, the relative frequency of contact from each source production type was calculated for each of recipient production farm types for direct contact based on swine movement (Appendix, Table S1) and relative frequency of sharing among production types for indirect contact based on truck sharing (Appendix, Table S2) information. Then the contact rates assigned to a production type were adjusted by multiplying the relative frequency by the maximum out-degree for that production type (Appendix, Table S3), where maximum out-degree is the maximum number of unique outgoing contacts an individual or group has in the population (Dubé et al., 2008). This approach of using the maximum out-degree between farms is thought to lead to a more realistic epidemic size, as opposed to using either the total number of shipments or average out-degree, which will tend to overestimate or underestimate the epidemic size respectively (Dubé et al., 2008). Indirect contact rates (Appendix, Table S4) from the truck sharing contact matrix were based on the maximum number of farms sharing a single truck within one week. The swine movement database used for this study did not have information for either continuous flow nursery farms or finishing farms. Direct contact rates for these production types were estimated based on expert judgement, which suggested that nurseryC and finishingC farm types receive one shipment per week from farrowing and

nurseryC farms respectively. Therefore, these values were used as the mean contact rate for nurseryC and finishingC production types. In addition, we assumed that the truck sharing patterns associated with these farms would be similar to those seen in nurseryA and finishingA farms.

Mean direct and indirect contact rates per week for each group are presented in Table 3.2. Disease transmission by direct contact was simulated in only those combinations of production types for which movement between the pairs was reported in the pilot swine movement study. Movement of pigs to farrowing and farrow-to-finish sites were not included in this study as some of these farms are closed farms and some farms typically receive animals from genetic or breeding farms but not from any of the production types considered in this study. However, transmission between farrowing and nurseryC as well as between nurseryC and finishingC were simulated, with contact rates being estimated as discussed earlier. For indirect contact, all combinations of production types were linked except for the case of farrow-to-finish with farrow-to-finish, as no truck sharing among these farm types was recorded in the swine movement data. There was no available information to parameterize the distance associated with pig movements between any two farms in Ontario, so the modelled distance distribution was based on experts' judgement using a BetaPERT distribution (Vose, 2008), with minimum, most likely and maximum distances of 0.5, 50 and 500 km. The minimum distance between farms corresponded to the minimum distance in the artificially generated random farm location data and the most likely coincided with the most likely distance distribution for most of the farms in the pilot swine movement study. In NAADSM, the contact between farms is influenced by geographical distance between two farms, however, the experts'

suggested that contact between farms is not limited by geographical distance, so a maximum of 500 km was chosen for the BetaPERT distribution. The same distance distributions were used for both direct and indirect contacts (Table 3.1), as indirect contact (truck sharing) between farms was also associated with pig movement.

3.3.6 Scenario Analysis

Two sets of scenarios (Set A and Set B: described below) were constructed. For each set of scenarios the transmission of PRRS virus by direct contact only or by both direct and indirect contacts was considered and simulated. Based on the production type of the initially infected farm, six scenarios for transmission by direct contact only (DC scenarios 1-6) and for transmission by both direct and indirect contact (D&IC scenarios 7-12) were created; resulting in a total of 12 scenarios for each set. The detailed combination of disease spread parameters, initially infected production type and duration of simulation is outlined in Table 3.3.

Set A scenarios

In these scenarios, we used the distribution of different production types within the swine industry as enumerated in Table 3.1 and which approximately matches the distribution of production types in Ontario, Canada in the recent past.

Set B Scenarios

Swine production in North America has undergone massive structural changes in terms of specialization to specific stages of production. These changes have led to the replacement of traditional farrow-to-finish type farms with a more vertically integrated production system and with increasing trends towards multisite production; changes driven by the need to increase efficiency and decrease production costs in an

increasingly competitive sector (Key and McBride, 2010). It is believed that this trend towards specialized pig production will continue and we wanted to evaluate the impact of these expected structural changes on the likely future spread of PRRS virus within swine production. Experts' judgement suggested that the proportion of farrow-to-finish farms in Ontario will decrease to around 30% (from 40% currently) of total farms in next five years. For Set B scenarios we randomly reassigned the 2552 farms into six production types where the proportion of farrow-to-finish farms was kept close to 30% (755 farms) and the proportions for the rest of the farm types were increased proportionately (farrowing: 350, nurseryA: 273, finishingA: 597, nurseryC: 182 and finishingC: 395 farms each). The remaining disease transmission parameters, mean rates of direct and indirect contact, and distance distributions between recipient units were identical to those used in Set A scenarios.

3.3.7 Sensitivity Analysis

Sensitivity analyses were performed for certain DC and D&IC scenarios in Set A. Scenarios in which epidemics were seeded in farrowing farms (Scenarios 1 and 7) were selected for sensitivity analysis, as they represented the worst-case scenario. We reduced the direct contact transmission probability from the baseline model (i.e. 1.0) to 0.75, 0.5 and 0.25 respectively. Similarly, to evaluate our assumption regarding indirect contact transmission probability, four sets of models with modified indirect transmission probabilities (0.03, 0.05, 0.25 and 0.5) were compared to the baseline model (0.1). To assess the impact of the assumed distance distribution between recipient units, eight models were run which modified the most-likely and maximum distances to the ranges of values (30, 40, 60, 70 km) and (300, 400, 600, 700 km) respectively. In all cases the

outputs were compared based on the proportionate change in median epidemic size relative to the baseline models.

3.4 Results

The distribution of overall epidemic sizes for each of the Set A scenarios are presented in Figure 3.2. The distribution of epidemic sizes for each of the six production types under each of the Set A scenarios are presented in Figure 3.3. Some quantitative differences were noted between the outputs from the Set A and Set B scenarios. However, there were limited differences between the distribution of epidemic sizes for the two sets and the quantitative differences observed were mainly due to variations in the distribution of the proportions of farms (see Appendix, Figures S1 and S2). Additionally, similar percentages of farms of each farm type were found to be infected for both Set A and B scenarios under corresponding DC and D&IC scenarios. As set B scenarios had similar patterns of outbreak, corresponding findings from these scenarios are presented in Appendix (Tables S5-S6) and only findings from Set A scenarios are discussed here in detail.

Overall, it was evident that simulations in which the infection was initiated in a farrowing farm resulted in much larger epidemic sizes for the DC scenarios (Figure 3a). For the D&IC scenarios (Figure 3b), infection initiated in farrowing farms still tended to infect a larger number of farms but the distribution of epidemic sizes (median and 95th percentile) were wider and the overlap between farrowing and other types of farms was large compared to narrower distributions in the DC scenarios with little overlap between farrowing and other types of farms. Additionally, outbreaks initiated from these farms infected a larger proportion of farms of other production types and for D&IC scenario

had impact on disease status of most of the production types, representing farrowing farms as "super-spreaders". Since epidemics initiated from farrowing farms constituted worst case scenarios, only descriptive results for these scenarios are presented, while descriptive results for rest of the scenarios are included in the Appendix. Descriptive statistics for median epidemic sizes (total and for each production type) and for number of infected farms (median and 95th percentile) and the median number of weeks required to reach the peak epidemic, for each of the DC and D&IC scenarios originating from farrowing farms are summarised in Table 3.4 (and in Appendix, Table S5 for additional Set A scenarios and Table S7 for Set B scenarios). Percentages of farms with and without any outbreak during the entire duration of simulation and percentage of nurseryA and finishingA farms that experienced multiple outbreaks during the simulation are summarized in Table 3.5 (and in Appendix Table S5 for additional Set A scenarios and Table S8 for Set B scenarios).

Variations in parameters of each scenario resulted in biologically plausible changes in the outputs of the model. Direct contact scenarios resulted in lower epidemic sizes than in models with D&IC, irrespective of production type of the farm in which the outbreak was initiated. Scenarios involving spread only by DC between farms resulted in outbreaks with median percentage of infected farms consisting of 31.5% and 37% of total farms, while for scenarios with D&IC, median percentage of infected farms were 42% and 49% of total farms respectively for Set A and B. By including indirect contact in the model, the median number of infected farms increased by 18% and 17% respectively for Set A and B scenarios than when only direct contact was used. Similarly, the median epidemic size increased by 44% (996 to 1431) and 43% (1170 to

1662) respectively for Set A and B scenarios when both direct and indirect contacts were incorporated in the model. Based on the percentage of farms infected for each production type, Table 3.5 (and Appendix Table S6 for additional scenarios), farrowing farms and farrow-to-finish farms were at least risk of becoming infected in DC scenarios, but infection was also spreading to farrowing farms when indirect contact was considered in the model. However, the proportion of infected farms was close to 1% for farrow-to-finish farms and did not increase above 4% for farrowing farms in either set of scenarios. FinishingA and finishingC farms were at the highest risk of receiving the infection, as more than 80% of finishing farms were infected in the DC scenarios, while the proportion infected increased to above 90% in the D&IC scenarios, indicating that these types of farms could be considered to be "super-receivers". Furthermore, nurseryC and finishingC farms had least impact on disease spread to other production types in the DC scenarios and resulted in much smaller epidemic sizes. Interestingly, with both direct and indirect contacts in the model not only did the epidemic size for outbreaks initiating from these production types increase, but the infection was also more likely to spread to all other production types. Models with DC reached the peak epidemic at 37 weeks indicating a slow progression of the outbreak compared to models with both D&IC, which reached the peak at 27 weeks. Some proportion of both nurseryA and finishingA farms were subject to multiple infection during the one year simulation and the proportions of farms with multiple outbreaks were higher when both direct and indirect contact were incorporated in the model.

The model outcome (median epidemic size) was quite sensitive to all of the input parameters of the direct and indirect contact transmission probability (Table 3.6).

However, it was not sensitive to any combination of distance distribution of pig movement investigated for sensitivity analysis (results not presented), suggesting that changes in distance distribution were negligible on the outcome of the model. For each input value of direct contact transmission probability in the DC baseline model, relatively similar proportionate decrease resulted in median epidemic size. For similar changes in direct contact transmission probability in the D&IC model, the resultant decrease in median epidemic size was smaller than with the DC model. Similarly, any decrease or increase in indirect contact transmission probability in the D&IC baseline model resulted in smaller proportionate decrease or increase in the median epidemic size respectively. While comparing D&IC scenarios, the outcome was more sensitive to changes in the value of direct contact transmission probability than to indirect contact transmission probability.

3.5. Discussion

To our knowledge, this is the first study carried out to simulate the between-farm spread of PRRS virus based upon the movement of infected animals in Canada. The incorporation of realistic contact structures between different production types in the Canadian swine industry was a notable, perhaps unique, aspect of this simulation study. The farms embedded in the model resemble the spatial distribution of swine farms across the province of Ontario (Ontario Pork Industry Council, 2013).

All sets of scenarios resulted in epidemiologically plausible outcomes. Epidemic size was smallest for scenarios which modelled only direct contact (DC). Epidemic sizes were larger and time to reach the peak epidemic shorter, for D&IC scenarios due to faster spread of infection via direct and indirect contacts. The incorporation of direct and

indirect contact in the model resulted in much larger outbreak sizes than the outbreaks produced by direct contacts or indirect contacts separately (results not shown), suggesting that the incorporation of both contact types had a non-linear effect on disease spread. Farrowing farms were at nominal risk when only direct contact was included in the model, corresponding to the fact that farrowing farms rarely experience the inward movement of pigs from farms of other production types considered in this study. When transmission by indirect contact was allowed in the model, the proportion of infected farrowing farms increased, suggesting that irrespective of the fact that they typically have no direct contact with other farms, they can still become infected through the sharing of transport vehicles. The total epidemic size increased by 44% and the number of infected farms increased by 18% in the D&IC models when compared to corresponding DC models; an increase due primarily to the sharing of trucks between farms. This finding highlights the importance of proper cleaning and disinfection of shipment trucks, which could result in preventing around half of the outbreaks and around one fifth of the farms from becoming infected.

Several contact network studies involving swine farms have demonstrated the hierarchical structure of the swine industry, where nursery and finishing farms must be considered to be highly vulnerable in terms of acquiring infection, while farrowing farms are the least vulnerable in terms of acquiring an infection but if infected become high risk farms for the on-going spread of any epidemic (Rautureau et al., 2012a; Büttner et al., 2013b; Dorjee et al., 2013). However, one contrasting finding from the present study was that when both direct and indirect contacts between farms were considered in the model, the hierarchical structure of the swine industry was no longer

such an important determinant in the spread of disease. The unidirectional spread of infection from one production type at the top level of hierarchy (farrowing and farrow-to-finish farms) to production types at lower levels (nursery and finishing farms) in direct contact models were significantly altered once the multidirectional spread of infection among all production types due to indirect contact was incorporated into the model. Additionally, in both the DC and D&IC scenarios, the median epidemic sizes were highest for epidemics that were initiated in farrowing farms. These findings suggest that any change in disease status of a farrowing farm can have a significant impact on all other production types, indicating that these farms are acting as "super-spreaders".

We simulated indirect contact as being based only on the sharing of trucks used for the shipment of pigs; ignoring all other forms of indirect contact between swine farms. This simplification is likely to have resulted in an under-estimation of the outbreak size. One of the key questions the study was attempting to answer was how best to quantify the spread of PRRS virus due to the movement of pigs; so incorporating only indirect contact associated with pig movement in the model seems reasonable. The currently implemented indirect contact matrix could be extended to include other potential sources of indirect contact between farms. In the current model, we did not consider movement of pigs to farrowing or farrow-to-finish farms, as some of these farms are closed farms while other farms that do replace animals from genetic or breeding farms that tend to maintain comparatively higher biosecurity standards and health status. However, this simplification may have resulted in underestimation of the epidemic size if any such movement occurred, particularly from infected genetic or breeding farms.

The PRRS virus possesses high genetic variability and rapid mutation in circulating strains is a commonly reported feature of the virus (Murtaugh et al., 1998; Han et al., 2006). Circulation of multiple strains and the emergence of a new strain to that assumed to have acted as the seed for an infection could cause multiple incursions on the same farm and have an impact on the overall dynamics of the spread of PRRS virus. The likely impacts of such scenarios were not evaluated in this study. Furthermore, we did not evaluate local or airborne spread of the virus; modes which have been reported in the case of PRRS virus transmission (Otake et al., 2002a). While these were considered to be beyond the scope of this study, the model could be further extended to incorporate local and/or airborne spread.

Reliability of the outcomes produced by models is assessed through model validation. However, in the absence of real outbreak data together with the corresponding historical between-farm movement data, external validation of any model is challenging. We believe that this model is based on a network that represents a realistic contact structure between swine farms in Canada, and most of the disease related parameters have been derived from peer-reviewed literature. However, it should be noted that estimates of contact frequency were based on a relatively small data set and that these data were collected in 2004. Additionally, regions from which the pig movement data were obtained were not identified in this paper, or in the original published report (Thakur et al., 2014), due to confidentiality restrictions. However the report included approximately half of the swine-producing regions of Canada and represented both Eastern and Western production system within Canada. It is thus our expectation that the contact data used in this study will not differ markedly from the production system in Ontario.

Another study analyzing swine movement data from Ontario {Dorjee, 2013 #78} have reported similar contact patterns, which supports our assumption that contact data used in this study is reflective of the swine production system in Ontario. Nevertheless, this model has highlighted the relative importance of direct and indirect contact via sharing of trucks, where trucks were not cleaned between successive shipments, in the transmission of PRRS virus. There are very few simulation studies of a similar nature against which to compare the findings of this study. A study evaluating the probable spread of PRRS virus in New Zealand was simulated using the InterSpread Plus software (InterSpread Plus, EpiCentre, Institute of Veterinary, Animal and Biomedical Sciences, Massey University, Palmerston North, NZ). This provides a similar platform to that which is available in NAASDM. This study estimated much smaller outbreaks with only around 1% of farms becoming infected during the first year and 5% farms becoming infected over 3 years of simulated production. However, this NZ study included a much higher proportion of non-commercial farms (92%) which typically have a very low mean direct contact rate (0.035/week) compared to the contact rates used in the present study (which ranged between 0.01-0.51/week). Also, as the index case was seeded in one of these non-commercial farms, the epidemic was unlikely to progress at a rapid pace. Additionally, the spatial distribution of farms may have a bearing on the spread of infection as well as the eventual extent of an outbreak. In a separate study, to compare model outputs from simulations using InterSpread Plus, NAADSM and AusSpread (Beckett and Garner, 2007) for foot and mouth disease, it was shown that these three modelling platform resulted in similar outcomes, indicating that differences in predictions are unlikely to be due to the use of a different modelling

platform or likely to be influenced by the population being modelled. One field study that aimed to investigate the impact of spatial proximity and network membership among farms on PRRS virus spread in Ontario has suggested that the risk of PRRS spread could be higher from sharing trucks than from being in close proximity to an infected farm (Arruda et al., 2014). A separate phylogenetic study of PRRS virus in North America has also revealed similarity among PRRS virus strains between farms at distant locations, which likely reflects the spread of the virus via direct and indirect contacts (Shi et al., 2013).

The parameter value for truck-related indirect contact transmission probability used in the model was largely based upon our assumptions and experts' judgement, as no literature could be found that attempted to quantify the probability of transmission of PRRS virus by indirect contact. In a transmission experiment, it was demonstrated that two out of five susceptible groups of pigs became infected via indirect contact with infected groups of pigs; however, distances between these groups of pigs was relatively short (Wills et al., 1997b). In similar models looking at the spread of foot and mouth disease virus, a transmission probability of 0.275 for vehicular contacts has been used (Bates et al., 2003). However, sensitivity analyses were performed to test the robustness of this assumption by decreasing and increasing the indirect contact transmission probability. These suggested that the model was not highly sensitive to either a decrease or increase in this parameter value.

Two other assumptions that we made were based on experts' advice, due to the unavailability of real data for this study. These related to the distribution in the proportion of farms of each production type and the distance distribution associated with

pig movements. The outputs from Set A and Set B scenarios indicated that varying the proportions associated with different farm types did not have a large impact on the pattern of the epidemics, and that the proportions of each farm type infected in Set A and Set B scenarios were similar. However, there were some differences in the epidemic size. Similarly, the approximate distance distribution used in our model did not influence the model outcomes, as negligible changes in the median epidemic size were observed under different combinations of distance distributions in the sensitivity analyses.

The assumption that when a single animal on a farm became infected, the whole farm was considered infected was reasonable, as it is quite unlikely that the virus become extinct without spreading to other animals on the farms given the virus is contagious and transmission studies have estimated R_0 of three for the transmission of virus among individual pigs (Nodelijk et al., 2000; Le Potier and Rose, 2012). However, these studies and some other sources of information have identified R_0 values between 1.8 and 14. One study reported the 95% CI between 2-6 (Nodelijk et al., 2000), while the other reported the 95% CI between 1.8-3.3. Similarly, one of the co-authors on this manuscript (ZP) has unpublished data that suggests that the R_0 could be anywhere between 2.5-14. In addition, with a mean shipment size of 130 animals, as reported in (Thakur et al., 2014) and with higher than 80% of animal level prevalence of PRRS virus (Nodelijk et al., 2003), it is more likely that more than one infectious animal will be present in a shipment from an infectious farm, therefore suggesting a negligible probability of infection extinction.

Farms in the swine industry have preferential and permanent contact structures. However, in this model, contacts among farms within the specified combination of production types were random. This is a limitation of the model and may have resulted in an over-estimation of outbreak size. However, in any modelling platform, we cannot totally avoid random contacts, as the members of each specific network within the model are likely to have contacts assigned randomly. Accounting for all possible forms of preferential contact structure would require the creation of several networks (contact groups) in the model making the model complex to simulate, and the results difficult to analyse or make general inferences from. Nevertheless, to minimize the effect on outbreak size, we used contact rates based on maximum out-degree between each pair of production types rather than based on the shipment frequency between pair of farms, which we believe have resulted in lower outbreak sizes than would be the case had shipment frequency been used to derive contact rates. We artificially restricted the locations of farms so that they were at least 0.5 km apart; in reality some farms may be situated closer than this, which may influence local spread of the virus. However, as we did not evaluate local spread of the virus in this study, the outcomes should not be influenced by this restriction. To evaluate the effect of using artificially generated farm locations on disease spread, we created three different sets of artificially generated farms, and found negligible differences in terms of the modelled distribution of outcomes based on simulations using these three sets of farm location. This suggested that the effect of using artificially generated farm locations had little impact on model outcomes.

Another limitation worth noting in the current study relates to the use of NAADSM. In that modelling framework it is not possible to select different farms in which to seed the infection while running multiple iterations; thus geographical proximity/remoteness of the initial 'source' farm may have a bearing on the extent of epidemic spread. However, this limitation is likely to have had limited impact on outcomes in the current study as the distance distribution set up allowed farms to contact others anywhere between 0.5 to 500 km, with the most likely distance being 50 km, and most farms were reachable within this distance distribution. Similarly, the assumption of setting the direct contact transmission probability to be 1.0 may have led to an over-estimation of epidemic size, as for some farms with AIAO production system, the virus may fade out before the end of production cycle. In addition to this, we used similar indirect contact rates for continuous flow farms to those observed for AIAO farms, due to non-availability of data for continuous flow farms. However, continuous flow farms might have higher direct contact rates than AIAO farms, therefore, such farms may likely also have higher indirect contact rates which might have resulted in an underestimation of the epidemic size. Finally, as some AIAO farms could have multiple barns and as the barns are in close proximity, the virus from one infected barn could spread to other barns via local or aerosol spread leading to a premise with longer infectious period or being persistently infected (Pitkin et al., 2009). Such AIAO farms with multiple barns are likely to have multiple outbreaks in this study with an over-estimation of epidemic size.

We attempted to run the baseline model until all infection was removed to determine the duration of an outbreak. However this condition did not arise even when the model was run for long time periods, indicating that with the specified contact rates and the

infectious duration of farms, farms in this study population will become endemic to PRRS once the virus is introduced, and fade-out is unlikely to occur at the population level of farms. To achieve complete fade-out, we speculate that either the closure of infectious farms or some restriction on direct and indirect contact would be required.

While an evaluation of control strategies was beyond the scope of this study, the results provide pointers as to those strategies that are most likely to be helpful in controlling the between-farm spread of PRRS virus. Avoiding direct contact with PRRS virus infected farms could have a significant impact in halting the spread of the virus. Reducing transmission via the sharing of trucks may require additional efforts, as previous truck movement details may not be readily available to any given farm. Two approaches that should reduce transmission of PRRS virus by indirect contact would be: (i) having dedicated transport vehicles between specific sets of farms (this will reduce the frequency of indirect contact); and, (ii) adopting proper cleaning and sanitation protocols for transport vehicles between successive shipments (this will decrease the transmission probability). Owing to the longer duration of virus survivability in cold weather, Dee and colleagues suggested rigorous cleaning and disinfection protocols for PRRS virus contaminated transport vehicles (Dee et al., 2004b; Dee et al., 2005a) which requires scraping out, high volume rinse, application of detergent, wash, disinfection and finally drying the vehicles. However, recent biosecurity studies in Canada suggest a low level of compliance to these protocols with only around one third of transport vehicles used for shipment of pigs being properly cleaned between successive shipments (Lambert et al., 2012b); which based on the results of the present study should be an issue of concern for the Canadian swine industry. Failure to comply with biosecurity

protocols for transport vehicles is also suggested to have impacted the current ongoing spread of porcine epidemic diarrhoea in North America (Lowe, 2014).

While infectious disease simulation models can produce measurable predictions, the strict quantitative interpretation of such model outcomes can be problematic; primarily due to the difficulty of incorporating all the relevant factors and accurately estimating the values of parameters and variables used in the model (Garnett, 2002). However, such models can still provide valuable qualitative insights, which can guide policy-making decisions. We have discussed some of the limitations of this model and have acknowledged the difficulty of validating the current model. However, the results of this model are epidemiologically plausible and have highlighted the important role that indirect contact via the sharing of trucks between farms can have on the between-farm transmission of PRRS virus.

3.6. Conclusion

This study provides insights into the patterns and likely extent of PRRS virus spread between swine farms in Ontario, Canada under several hypothetical scenarios, incorporating both direct and indirect contact. The current model has highlighted the relative importance of direct and indirect contact via sharing of trucks, where trucks were not cleaned between successive shipments, on between-farm transmission of PRRS virus. The results suggest that hypotheses regarding the vulnerability of swine farms related to the hierarchical structure of a typical swine production system may not hold true when indirect contact among production types are considered. This model was not intended for quantitative prediction and hence any such interpretation of the outputs from the model should be made with caution. Nevertheless the findings from this study

should be considered a qualitative guide to understand the pattern and magnitude of likely PRRS outbreaks under the scenarios explored. Further development of this model may be helpful in the evaluation of additional what-if scenarios related to PRRS virus spread and in identifying effective control strategies to prevent the spread of PRRS virus.

3.7 References

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Table 3.1 Model parameters used for simulation of between farm spread of PRRS virus

Parameters	Value	Reference
Total Farms (N)	**2552**	Agriculture census-2011
Farrow-to-finish (FF) farms	1012 (39.6%)	
Farrowing (F) farms	306 (12%)	
AIAO Nursery Farms (NurseryA)	248 (9.7%)	
AIAO Finishing Farms (FinishingA)	494 (19.3%)	
CF Nursery Farms (NurseryC)	166 (6.5%)	
CF Finishing Farms (FinishingC)	326 (12.9%)	
Transmission Probability	1 (direct contact)*	(Neumann et al., 2007)
	0.1 (indirect contact)*	assumed
Infectious Duration (week)		
Farrow-to-finish farms	Whole duration of simulation	(Neumann et al., 2007)
Farrowing farms	Whole duration of simulation	(Neumann et al., 2007)
NurseryA Farms	4.5 weeks	Expert judgement[1]
FinishingA Farms	Uniform (12,15) weeks	Expert judgement[1] (Kuipers and Niederreiter, 2012)
NurseryC Farms	Whole duration of simulation	(Neumann et al., 2007)
FinishingC Farms	Whole duration of simulation	(Neumann et al., 2007)
Distance of recipient units	BetaPERT (0.5,50,500)	Expert judgement[1] (Vose, 2008)

*for all six production types

[1]Two co-authors of this manuscript (DH and ZP) provided expert opinion to estimate these parameters.
AIAO=All in all out; CF=Continuous flow.

Table 3.2 Description of contact structure used for simulation of between-farm spread of PRRS virus

Contact Groups	Mean Contact rate/week[1]	
(Source - Destination)	Direct	Indirect
FF - FF	-	-
FF - F	-	0.0007
FF - NurseryA	0.06	0.002
FF - FinishingA	0.17	0.004
FF - NurseryC	-	0.002
FF - FinishingC	-	0.004
F - FF	-	0.0007
F - F	0.01	0.03
F - NurseryA	0.51	0.01
F - FinishingA	0.03	0.002
F - NurseryC	1	0.01
F - FinishingC	-	0.002
NurseryA - FF	-	0.002
NurseryA - F	-	0.012
NurseryA - NurseryA	0.03	0.03
NurseryA - FinishingA	0.31	0.05
NurseryA - NurseryC	-	0.03
NurseryA - FinishingC	-	0.05
FinishingA - FF	-	0.004
FinishingA - F	-	0.002
FinishingA - NurseryA	0.01	0.05
FinishingA - FinishingA	0.21	0.16
FinishingA - NurseryC	-	0.05
FinishingA - FinishingC	-	0.16
NurseryC - FF	-	0.002
NurseryC - F	-	0.012
NurseryC - NurseryA	-	0.03
NurseryC - FinishingA	-	0.05
NurseryC - NurseryC	-	0.03
NurseryC - FinishingC	1	0.05
FinishingC - FF	-	0.004
FinishingC - F	-	0.002
FinishingC - NurseryA	-	0.05
FinishingC - FinishingA	-	0.16
FinishingC - NurseryC	-	0.05
FinishingC - FinishingC	-	0.16

[1]mean contact rates calculated based on maximum out-degree between production types
F=Farrowing, FF=Farrow-to-finish , NurseryA= All in all out Nursery, NurseryC=Continuous flow Nursery, FinishingA= All in all out Finishing, FinishingC=Continuous flow Finishing

Table 3.3 Descriptions of scenarios used for simulation of between farm spread of PRRS virus[1]

Scenario Number	Scenario Name	Spread by Direct Contact[a]	Spread by Indirect Contact[b]	Transmission Probability		Movement Restriction	Initially infected production type	Duration of simulation
				Direct Contact	Indirect Contact			
1	DC_F	Yes	No	1	NA	No	Farrowing	52 weeks
2	DC_NA						NurseryA	
3	DC_FiA						FinishingA	
4	DC_FF						Farrow-to-finish	
5	DC_NC						NurseryC	
6	DC_FiC						FinishingC	
7	D&IC_F		Yes		0.1		Farrowing	
8	D&IC_NA						NurseryA	
9	D&IC_FiA						FinishingA	
10	D&IC_FF						Farrow-to-finish	
11	D&IC_NC						NurseryC	
12	D&IC_FiC						FinishingC	

[1]Same combination of parameters were used for Set B scenarios (No. 13- 18 DC and N0. 19- 24 D&IC scenarios) with the difference in distribution of proportion of farm types, [a]spread of disease from one farm to another via movement of infected animals, [b]spread of disease from one farm to another through sharing of trucks for shipment of pigs, TP=Transmission Probability, DC=Direct Contact, D&IC=Direct and indirect contact, F=Farrowing, NA=NurseryA, FiA=FinishingA, FF=Farrow-to-finish NC= NurseryC, FiC=FinishingC

Table 3.4 Descriptive summaries of the model-generated number of farms infected with PRRS virus and time required to reach the peak epidemic from a simulation based on 1000 iterations of scenarios 1 and 7 (Set A scenarios)

Scenario No.	Scenario Name	Farms Infected: Median (p95)							Epidemic Size: Median (p95)			Week to peak epidemic (p95)
		Overall	Farrowing	Nursery A	Finishing A	Farrow-to-finish	Nursery C	Finishing C	Overall	Nursery A	Finishing A	
1.	DC_F	802 (892)	1(4)	75 (97)	408 (434)	0 (0)	40 (72)	280 (308)	996 (1143)	93 (129)	583 (677)	39 (49)
7.	D&IC_F	1061 (1125)	12 (21)	150 (174)	457 (468)	9 (15)	115 (138)	318 (322)	1431 (1579)	233 (297)	746 (820)	27 (43)

DC=Direct Contact, D&IC=Direct and indirect contact, F=Farrowing,

For median number of farms infected, farms that had multiple infections were counted only once; while for median epidemic size, farms with multiple outbreaks were counted multiple times. For Farrowing, Farrow-to -finish, NurseryC and FinishingC farms, the median epidemic sizes were similar to their respective median numbers of farms infected. NurseryA= All in all out Nursery, NurseryC=Continuous flow Nursery, FinishingA= All in all out Finishing, FinishingC=Continuous flow Finishing

p95= 95th percentile

Table 3.5 Summary statistics relating to multiple outbreaks of PRRS virus during the period of simulation based on 1000 iterations of scenarios 1 and 7 (Set A scenarios)

Scenario No.	Scenario Name	Percentage of farms with the indicated number of outbreaks													
		Farrowing		NurseryA				FinishingA			Farrow-to-finish		NurseryC		FinishingC	
		0	1	0	1	2-3	>4	0	1	2-3	0	1	0	1	0	1
1	DC_F	99.7	0.30	69.8	24.2	6.0	0	17.4	50.8	31.8	100	0	75.9	24.1	14.1	85.9
7	D&IC_F	96.1	3.9	39.5	35.9	23.0	1.6	7.9	40.0	52.1	99.1	0.9	30.8	69.2	2.5	97.5

DC=Direct Contact, D&IC=Direct and indirect contact, F=Farrowing, NurseryA= All in all out Nursery, NurseryC=Continuous flow Nursery, FinishingA= All in all out Finishing, FinishingC=Continuous flow Finishing

Table 3.6 Sensitivity analysis of the median epidemic size of simulated PRRS virus outbreaks to direct and indirect contact transmission probabilities in a population of 2552 swine farms

Scenarios	Parameters		± % change in input parameter		Epidemic Size: Median (p5-p95*)	% change in median outcome compared to baseline
	DCTP[a]	ICTP[b]	DCTP[a]	ICTP[b]		
1. DC_F	**1**	**NA**	**Baseline Scenario**		**996 (830-1143)**	
DC-F with change in DC TP to 0.75	0.75	NA	-25	0	649 (469-810)	-34.8
DC-F with change in DC TP to 0.5	0.5	NA	-50	0	277 (195-418)	-72.2
DC-F with change in DC TP to 0.25	0.25	NA	-75	0	85 (51-133)	-91.5
7. D&IC_F	**1**	**0.1**	**Baseline Scenario**		**1431 (1297-1579)**	
D&IC-F with change in DC TP to 0.75	0.75	0.1	-25	0	1140 (984-1291)	-20.3
D&IC-F with change in DC TP to 0.5	0.5	0.1	-50	0	721 (546-895)	-49.6
D&IC-F with change in DC TP to 0.25	0.25	0.1	-75	0	241 (129-391)	-83.2
7. D&IC_F	**1**	**0.1**	**Baseline Scenario**		**1431 (1297-1579)**	
D&IC-F with change in IC TP to 0.5	1	0.5	0	400	2991 (2797-3152)	109
D&IC-F with change in IC TP to 0.25	1	0.25	0	150	2194 (2005-2370)	53.3
D&IC-F with change in IC TP to 0.05	1	0.05	0	-50	1268 (1118-1428)	-11.4
D&IC-F with change in IC TP to 0.03	1	0.03	0	-70	1169 (968-1243)	-18.3

[a]Direct Contact Transmission Probability, [b]Indirect Conatct Transmission Probability

*p5 = 5th percentile, p95 = 95th percentile

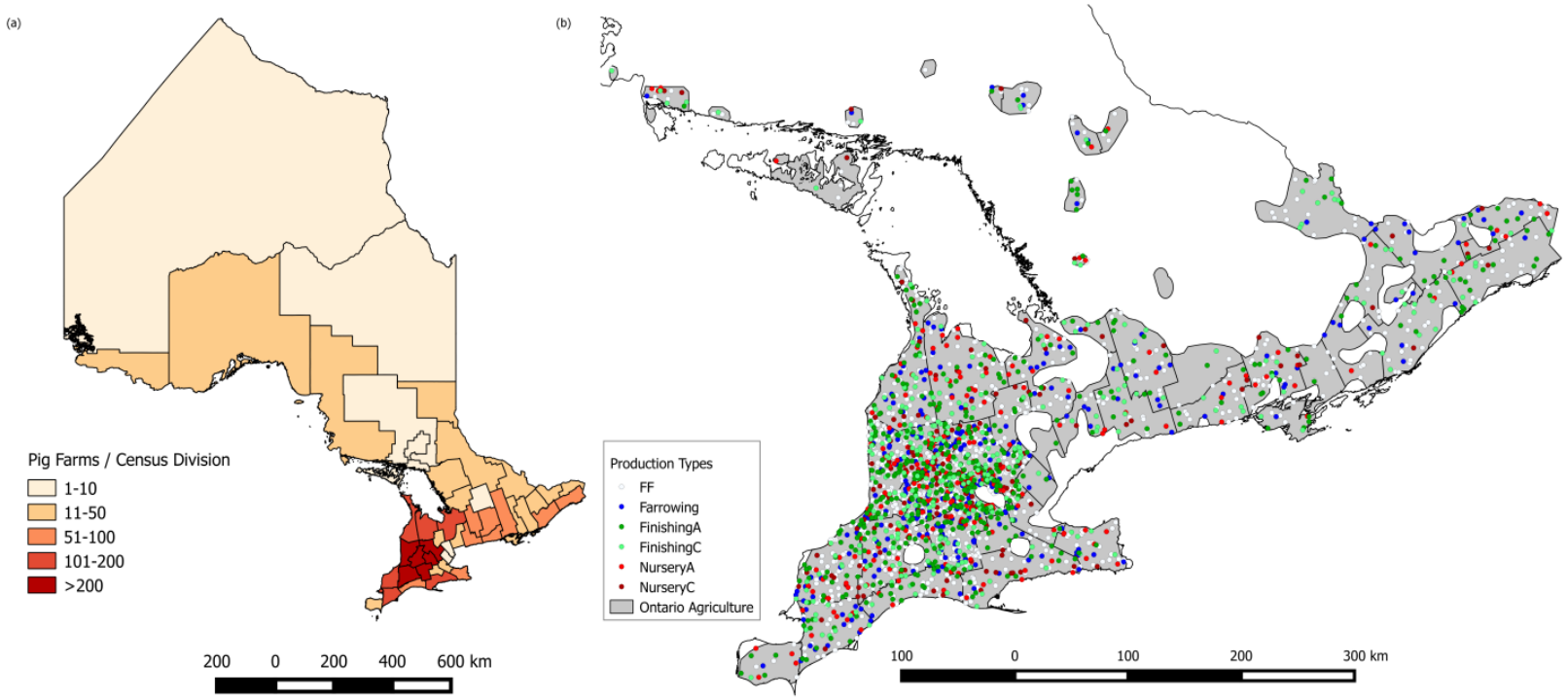

Figure 3.1 Density of pig farms in each census division of Ontario (a), and spatial distribution of swine farms of six production types (with artificially generated locations based on information provided in agriculture census) used in the simulation of between - farm spread of PRRS virus among Ontario swine herds illustrated by production type (b). Legend: Ontario Agriculture=Agricultural Land Parcel of Ontario, FF=Farrow-to-finish, NurseryA= All in all out Nursery, NurseryC=Continuous flow Nursery, FinishingA= All in all out Finishing, FinishingC=Continuous flow Finishing

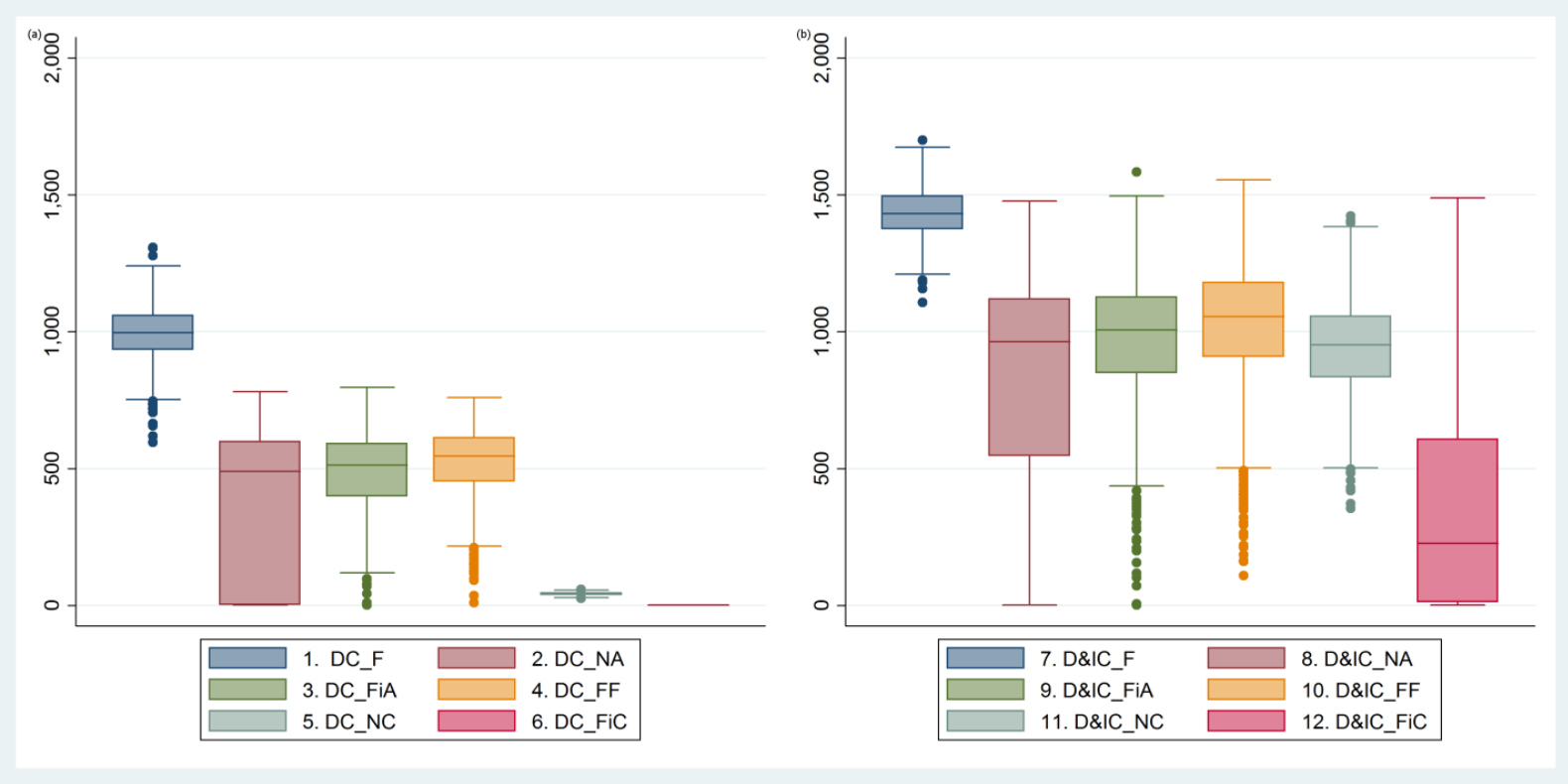

Figure 3.2 Distribution of the overall epidemic size of PRRS virus simulated outbreaks of between-farm spread among swine herds of Ontario under assumptions of direct (a) and direct and indirect contacts (b) between farms for Set A scenarios. Different colors represent outputs from scenarios in which the epidemic was initiated from farm of the noted production type. DC=Direct Contact, D&IC=Direct and indirect contact, F=Farrowing, NA=NurseryA, FiA=FinishingA, FF=Farrow-to-finish NC= NurseryC, FiC=FinishingC

The middle band of the box represents the 50th percentile, the bottom and top of the box represents 25th and 75th percentile and the end of the whiskers represent maximum and minimum within ±1.5 interquartile range of the epidemic size distribution.

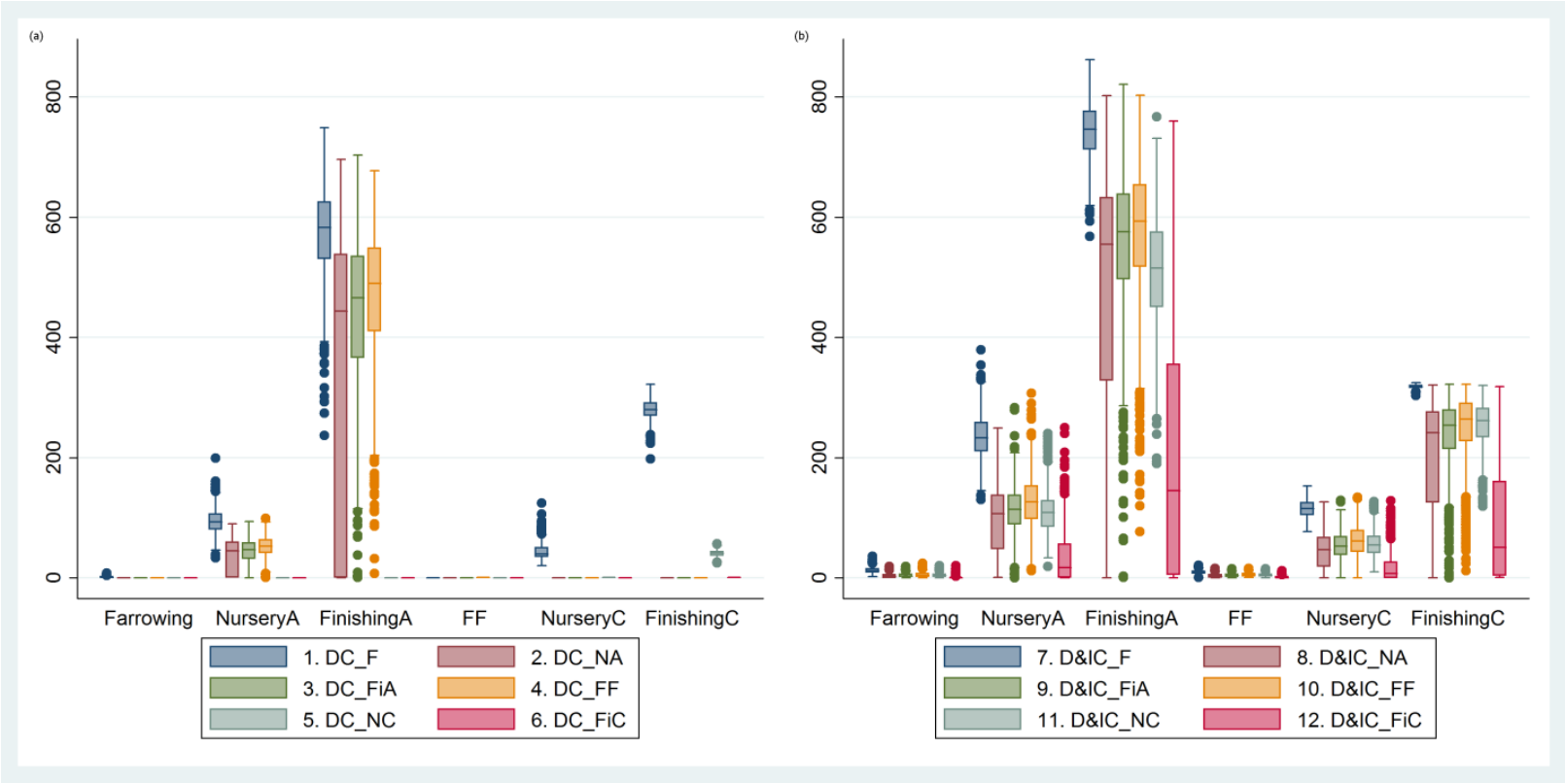

Figure 3.3 Distribution of epidemic size of PRRS virus simulated outbreaks by swine production type among swine herds of Ontario under assumptions of (a) direct and (b) direct and indirect contact between farms for Set A scenarios. Different colors represent scenarios in which farms of the indicated production type were the initially infected premises. DC=Direct Contact, D&IC=Direct and indirect contact, F=Farrowing, NA=NurseryA, FiA=FinishingA, FF=Farrow-to-finish NC= NurseryC, FiC=FinishingC

The middle band of the box represents the 50th percentile, the bottom and top of the box represents 25th and 75th percentile and the end of the whiskers represent maximum and minimum within ±1.5 interquartile range of the epidemic size distribution.

Chapter 4 Development of a network based model to simulate the between-farm transmission of the Porcine Reproductive and Respiratory Syndrome virus

4.1 Abstract

Recent studies have suggested that contact structure within a population can significantly affect the outcomes of infectious disease spread models. The objective of this study was to develop a network based simulation model for the between-farm spread of porcine reproductive and respiratory syndrome virus to assess the impact of contact structure on between-farm transmission of PRRS virus. For these farm level models, a hypothetical population of 500 swine farms following a multistage production system was used. The contact rates between farms were based on a study analyzing movement of pigs in Canada, while disease spread parameters were extracted from published literature. Eighteen distinct scenarios were designed and simulated by (1) varying the mode of transmission (direct versus direct and indirect contact), (2) type of index herd (farrowing, nursery and finishing), and (3) the presumed network structures among swine farms (random, scale-free and small-world). PRRS virus was virtually seeded in a randomly selected farm and 500 iterations of each scenario were simulated for 52 weeks. The median epidemic size by the end of the simulated period and percentage die-out for each scenario, were the key outcomes captured. Scenarios with scale-free network models resulted in the largest epidemic sizes, while scenarios with random and small-world network models resulted in smaller and similar epidemic sizes. Similarly, stochastic die-out percentage was least for scenarios with scale-free networks followed by random and small-world networks. Incorporation of indirect contact via sharing of trucks between farms resulted in a significant increase in the epidemic size for all scenarios, compared to when only direct contact was included in the model. Findings of the study indicated that incorporating network structures among the swine

farms had a considerable impact on the spread of PRRS virus, highlighting the importance of understanding and incorporating realistic contact structures when developing infectious disease spread models for similar populations. The study further suggested that irrespective of network structure considered, the indirect contact played a significant role in further spreading the infection to swineherds in the population.

4.2. Introduction

Porcine reproductive and respiratory syndrome (PRRS) is a viral disease of swine with worldwide distribution which affects all swine production stages and has a major economic impact on the swine industry (Neumann et al., 2005; Holtkamp et al., 2007). PRRS is caused by an enveloped, spherical, single stranded, positive-sense RNA virus of family Arteriviridae (Cavanagh, 1997). The virus presents significant antigenic and molecular variability suggesting two distinct genotypes: Type I (European genotype) and Type II (North American genotype). Wide genotypic variation within each genotype has also been reported (Wensvoort et al., 1992; Nelson et al., 1993; Murtaugh et al., 1995). PRRS is characterised by late-term abortions, still-births, mummified and weak piglets in breeding herds, increased mortality rates in piglets in addition to respiratory disease and poor growth performance and mortality in growing pigs (Nodelijk, 2002). Several mechanisms for transmission of the virus between farms have been proposed; the most important of which is the introduction of infected animals or semen (Yaeger et al., 1993; Mortensen et al., 2002). Mechanical transmission by contaminated vehicles and fomites, as well as local transmission by aerosols, has also been reported (Dee et al., 2002c; Otake et al., 2002c; Dee et al., 2004d; Holtkamp et al., 2010).

The use of computer models to simulate the spread of infectious disease in various livestock industries has been increasing and is an important tool for researchers and policy-makers to understand the likely magnitude of probable outbreaks and to explore scenarios to determine the efficiency of possible control measures such as vaccination, movement restriction, etc. (Morris et al., 2001; Riley et al., 2003; Kiss et al., 2006a; Francis et al., 2010). Model outputs are supportive in emergency preparedness and in informed decision making (Ferguson et al., 2001; Morris et al., 2001). The representativeness of the simulation model and effectiveness of the plans developed based on model outcomes are highly dependent on the validity of underlying model assumptions and the accuracy of the parameters incorporated in these simulations (Francis et al., 2010). Most of the infectious disease spread models that use traditional differential equations (May, 1995; Rahmandad and Sterman, 2008) fail to account for the chance nature of epidemic spread (randomness/stochasticity) as well as heterogeneity in contact among individuals within a population (Dangerfield et al., 2009). Incorporating such stochasticity and individual heterogeneity (variations in age, sex, production types, contact rates etc.) can greatly increase the complexity of models. Recent increases in computational power has led to the increased use of Agent-Based Models (ABM); these models can account for stochasticity as well as heterogeneity in individual attributes. In addition, ABMs can be extended to incorporate contact heterogeneity among individuals and various network structures that are present in the populations can also be modelled (Rahmandad and Sterman, 2008; Lanzas and Chen, 2014).

For many infectious diseases, including PRRS, transmission occurs mainly by direct or indirect contact between individuals. Thus disease is spread by a network of contacts (movement of infectious animals) such that the probability of spread of infection is limited to a finite set of susceptible contacts in contrast to the assumption of mass-action models or homogenous compartmental models, in which every susceptible individual in the population has the same number of contacts and thus every individual in the population has similar probability of becoming infected (Keeling, 2005). Incorporating network structure into disease spread models allows for the computation of population level epidemic dynamics by capturing interactions at the individual level. Network graphs, the concept of which originated from graph theory, have been used to model contact patterns among animal holdings where animal holdings are represented as nodes and movement between the nodes construct the edges. Realistic contact networks of animal movement such as those generated by utilizing characteristics from actual contact can further be utilized to simulate the spread of disease via movement of animals (Keeling and Eames, 2005a). Several studies analyzing the movement of pigs between farms in different geographical regions of the world have provided insights into understanding network structure among swine farms and such networks have demonstrated the presence of both small-world and scale-free topologies (Bigras-Poulin et al., 2007; Rautureau et al., 2012b; Büttner et al., 2013b; Dorjee et al., 2013; Thakur et al., 2014). In recent years, simulation of infectious disease spread within a number of theoretical networks have provided insights into understanding the likely pattern of disease spread in populations with that particular type of contact network characteristics (Watts and Strogatz, 1998; Moore and Newman, 2000; Pastor-Satorras and Vespignani,

2001; Eames and Keeling, 2002; Neal, 2003; Rahmandad and Sterman, 2008; Rahmandad et al., 2011). Similarly, some other studies have utilized real-world (empirical) network structures to simulate disease spread and to evaluate the impact of the network characteristics of the population on likely spread of a number of infectious disease of humans (Eames and Keeling, 2002; Rahmandad et al., 2011) and animals (Kao et al., 2006; Kiss et al., 2006a; Ayyalasomayajula et al., 2008a; Kiss et al., 2008; Álvarez et al., 2011; Duncan et al., 2012; Tinsley et al., 2012; Dürr et al., 2013; Carne et al., 2014).

To the best of our knowledge, there have not been any published simulation models that incorporate contact heterogeneity among swine herds or which explore the assumptions regarding network structures with the swine industry that seek to evaluate the between-herd spread of PRRS virus, . Recent studies on swine movement in Canada have provided insight into the contact structures of the swine industry in Canada (Dorjee et al., 2013; Thakur et al., 2014). The swine industry in general possesses a specialized production system with a hierarchical structure, where pigs are moved from one production type to another during different stages of their growth. With the availability of these inputs (network structure and contact parameters), we recognized that the opportunity existed to create a network based model that explicitly considered stochasticity and individual contact structures to enhance our understanding of PRRS virus spread. The objective of this study were to develop a network based simulation model for the between-farm spread of PRRS virus to assess the impact of network structure on between-farm transmission of PRRS virus.

4.3. Materials and Methods

4.3.1 Study Population

A hypothetical population of 500 swine farms, that followed a specialized multistage production system, was generated and used for the simulations. The distribution of farms to each of the three production types (farrowing, nursery and finishing) are presented in Table 4.1. All swine farms included in this study belonged to one of three production types: (1) farrowing farms, which produce piglets that are delivered to nursery farms after weaning (at around 3 weeks of age); (2) nursery farms, where pigs are reared after they are weaned but before the fattening stage (approximately 3-8 weeks); and (3) finishing farms, where pigs above 8 weeks of age are grown till market age. The proportion of farms in each production type were assigned based on the observed proportion of farms found in swine movement data from four Canadian provinces (Thakur et al., 2014). For the sake of simplicity, nursery and finishing farms were considered to have adopted all-in-all-out (AIAO) practice by site, where pigs are moved in or out of the premises in a batch and the premises are expected to be properly cleaned and disinfected and kept empty for a certain duration before a new replacement batch of pigs is introduced.

4.3.2 The Network Models

To assess the impact of network structure on between-herd transmission dynamics of PRRS virus, a stochastic , network-based, farm-level, state transition computer simulation model was developed in AnyLogic® (Version 7.0.1, XJ Technologies, Russia) .

At the beginning of each iteration, one randomly selected farm was seeded with PRRS virus, which in turn became infectious. The rest of the farms were susceptible to the virus at the beginning of the simulation. The randomly seeded farm could spread infection to connected farms by the shipment of pigs (direct contact) or to any random farm via the sharing of trucks (indirect contact). Farrowing farms became infectious once they received shipments from infected farrowing or finishing farms or if they shared trucks with any other infected farm, though with a much lower probability than was the case for direct contact. Once infectious, farrowing farms remained infectious throughout the model run following a Susceptible-Infectious (SI) state transition, as represented in Figure 4.1. Nursery and finishing farms were allowed to become infectious in similar ways, either by shipment of pigs from connected farrowing farms and from connected farrowing or nursery farms respectively and also through the sharing of trucks with any infected farm. These farms remained infectious for a certain duration (4.5 weeks for nursery farms and between 12-15 weeks for finishing farms) and then were allowed to recover for a two weeks downtime period for farms practicing AIAO system. After this period the farms were assumed to be susceptible, thus following a Susceptible-Infectious-Recovered-Susceptible (SIRS) state transition approach.

4.3.3 Network Structure

The three network structures in which spread of PRRS virus was explored in this study were: random, small-world and scale-free (Figure 4.2). The random network is considered a theoretical network. The other two network structures (small-world and scale-free) were selected because most of the swine movement networks studied have

demonstrated the presence of small-world and scale-free topologies (Nöremark et al., 2011b; Rautureau et al., 2012a; Büttner et al., 2013b; Dorjee et al., 2013; Thakur et al., 2014). We used the inbuilt features of AnyLogic to simulate these three types of networks, which were constructed based on algorithms described for each of random (Erdős and Rényi, 1960), small-world (Watts and Strogatz, 1998) and scale-free (Barabási and Albert, 1999) networks. The construction rules that were employed to build each of the three types of networks are summarised below.

The random network is characterized by each node having equal number of contacts and, where each node has equal probability of having a contact with any other node in the network. This is analogous to the assumption of homogenous mixing of individuals in a population and will result in a network characterized by low clustering coefficient and high average path length, where clustering coefficient is defined as the proportion of closed triplets (formed by 3 farms connected by 3 undirected links) to total number of open (formed by 3 farms connected by 2 undirected links) and closed triplets in the network and average path length is defined as the average number of links along the shortest or geodesic paths between all possible pairs of nodes in the network (Dubé et al., 2009). The random network for 500 (N) farms with an average of two connections per farm (k) was generated by randomly selecting k*N/2 of the N(N-1)/2 possible links in N nodes, which yielded a Poisson distribution for the number of connections each farm had with a mean of 2 (Rahmandad et al., 2011).

The small-world network, a widely used topology considered to more accurately represent many real-world situations, has many local and some long-distance links and is characterized as having relatively larger clustering coefficients and shorter average

path lengths than that of random networks of similar size. A small-world network may be constructed from a ring-lattice network by randomly rewiring a proportion of links to have long-range connections in the network. The probability of such long-range links, as described by Watts (Watts, 2003), should be around 0.05. However, with this probability of long-range connections given a population of 500 farms with an average of two connections per farm, the clustering coefficient and average path length obtained were similar to that of a random network. We evaluated a set of long-range connection probabilities that would yield approximately similar network characteristics to those observed in real swine movement networks. Using a probability of 0.5, the resultant clustering coefficient (0.02) obtained was closer to, but still smaller than, that which was observed in the analysis of swine movement networks in Canada (Dorjee et al., 2013; Thakur et al., 2014), though the average path length was greater than in the observed networks. The average path length for the simulated networks could not be decreased further to match that seen in the observed networks and so we decided to use a probability of 0.5 for long-range connections to simulate small-world networks, as this probability yielded the closest match to the observed network.

In scale-free networks, most of the individuals have a limited number of connections while a few individuals are highly connected (Keeling and Eames, 2005a). Scale-free networks are characterized by right-skewed distribution for the number of contacts in the network, where the number of contacts follow a power-law distribution (Barabási et al., 2000).The scale-free networks were build using the preferential attachment algorithm (Barabási and Albert, 1999) in which the probability of linking a new node to existing nodes is proportional to the number of links each node already has. Preferential

attachment yields a power law for the probability that a node has k links with a scaling parameter γ, where prob (k) $=\alpha k^{-\gamma}$. Empirical studies typically show $2 \leq \gamma \leq 3$. A fixed value of $\gamma=3$ was used in this simulation model based on an analysis of swine movement data in Canada (Dorjee et al., 2013; Thakur et al., 2014).

Analyses of swine movements are reflective of the structure of swine industry and indicate directional flow from farrowing farms to nursery farms and from nursery farms to finishing farms with small proportions of movements between farrowing farms (Rautureau et al., 2012a; Dorjee et al., 2013; Thakur et al., 2014). We used similar approaches to connect farms of all three production types. Since it is not possible to specify directional linkage between individual entities in AnyLogic the directionality of pig movements was implemented by specifying unidirectional messaging between objects dependent on their class membership. For example, farrowing farms were allowed to general contact ‘messages’ to nursery farms but nursery farms were not allowed to contact farrowing farms (Figure 4.2). Similarly, for indirect contact as well the flow of "messages" was directional such that any farm sharing a truck with only an infected farm had the chance to get infected.

Finally, the default system for network construction in AnyLogic creates links amongst all farms (nodes) regardless of production type. However, in the swine industry nursery farms and finishing farms are not usually connected with other nursery and finishing farms. This restriction was imposed onto the simulated networks by customizing the default AnyLogic code such that it disconnected links between nursery or finishing farms; such links were then rewired randomly to either farrowing or finishing farms for nursery farms and to farrowing or nursery farms for finishing farms. After doing so, it

was ascertained that the characteristics (clustering coefficients, average connection and scaling parameter) of each of the rewired networks were preserved.

4.3.4 Parameters

The parameters used to build the network based AnyLogic models are summarized in Table 4.1.

(a) Disease duration

The infectious durations for nursery and finishing farms were based on the assumptions on duration of stay of pigs in these production types. Farms using the AIAO system of production are assumed to clear any infection with the turnout of each batch of pigs, by proper cleaning and disinfection of premises as well as allowing a minimum downtime period before the introduction of a new batch of pigs. However, in farrowing farms, new susceptible animals are continuously produced and replaced, which allows the virus circulate in the farm and to persist for long periods (Nodelijk et al., 2003). We assumed an infectious duration of one year for this type of farm, similar to that specified by Neumann et al. (2007).

(b) **Transmission probabilities**

The direct and indirect contact transmission probabilities and infectious duration for farms in each of the three production types were similar to that used in a separate simulation study on PRRS virus spread using the North American Animal Disease Spread Model (Thakur et al., 2015). A direct contact transmission probability of 1.0 was used, as was reported by Neumann et al. (2007). The probability that a farm could become infected via indirect contact was set at 0.1; an order of magnitude lower than the

probability associated with the movement of infected pigs, and was based on the authors' judgement and impact of this assumption was evaluated in sensitivity analysis.

(c) Contact Rates

Direct contact in these models was defined as the movement of at least one pig from one farm to another. The direct contact rates among farms of these production types were derived from analyses of swine movement in four Canadian provinces (Thakur et al., 2014) and are described in a separate study (Thakur et al., 2015). Swine movement studies in Canada have reported a negligible proportion of movement of pigs going to farrowing farms (Dorjee et al., 2013; Thakur et al., 2014). However, experts that the authors consulted with noted that while some farrowing farms are closed herds and replace breeding animals only from within the farm, other farrowing operations do replace breeding pigs from finishing farms or from specialized breeding or genetic farms. To account for such replacement from external sources we assumed that some farrowing farms would replace gilts from finishing farms and based on experts suggestions, a mean direct contact rate reflecting such replacement was set to 0.25/week (Table 4.2).

Indirect contact in these models was based on contacts between farms that occurred due to the sharing of transport vehicles between farms for the purpose of the shipment of pigs. The indirect contact rates were based upon the proportion of trucks sharing among farms of each production type and were obtained from the same study from which direct contact rates between farms are obtained (Thakur et al., 2014; Thakur et al., 2015). The mean direct and indirect contact rates between farms of each production types are presented in Table 4.2.

4.3.5 Assumptions

In this study, we assumed that all farms were free of PRRS virus at the beginning of the simulation. We also assumed that the strain of PRRS virus that initiated the outbreak did not mutate during the course of the simulation. The within-herd dynamics of PRRS virus spread were ignored such that when a single animal on a farm became infected, the entire farm was considered infectious. We further assumed that in any outgoing shipment from an infectious farm at least one infected animal would be present in the shipment, so that when a shipment occurs from an infected farm, the probability for transmission of the virus was assumed to be one. For indirect contact, we included only the sharing of transportation vehicles between farms for shipment of incoming or outgoing animals and ignored all other forms of indirect contact, such as the movement of personnel or the sharing of other equipment. For calculation of indirect contact rate, when two farms already had direct contact, the sharing of trucks inherent in such a contact was not counted again towards indirect contact. Moreover, we assumed that such trucks were not adequately cleaned and disinfected between successive shipments so as to remove the potential of virus spread, though the transmission probability was considerably lower than was the case for direct contacts. Lastly, in order to assess the impact of the three network topologies on PRRS virus spread, farms were assumed to be identical in terms of farm size, breed and management practices.

4.3.6 Scenario Analysis

For each of the three network models, transmission of the PRRS virus by direct contact only as well as by both direct and indirect contacts was considered and simulated. Additionally, the impact of the production type of initially infected farm on the epidemic was also evaluated. Eighteen different scenarios were constructed based on the three

network types (scale-free, random and small-world); two modes of transmission of the virus: by direct contact only (DC scenarios) and by both direct and indirect contact (D&IC scenarios); and one of the three production types for the farm from which the epidemic started. The combination of network type, mode of disease spread and initially infected production type, is detailed in Table 4.3.

4.3.7 Model Outcomes

In each model run, the spread of PRRS virus in the population was initiated by randomly seeding infection at time zero in a single farm. The time unit for simulation was one week and the model was run for 52 weeks. A 52 week simulation duration was selected based on the infectious duration period for farrowing, so that the spread of the virus during one infectious cycle of such farms can be understood. Five hundred iterations of each scenario were run to generate a distribution of predicted outcomes. The transmission dynamics of PRRS virus for all network types under each pre-specified condition were summarized, compared and evaluated. After simulation of each scenario, the following model outputs were reported: **Epidemic Size:** The total number of infected farms during a given simulation; **Die-out percentage:** Percentage of total iterations in which the infection does not progress from the initially seeded farm to at least five other farms (i.e. if less than 1% of all farms became infected a 'die-out' due to the stochastic nature of the simulation was noted); **Peak week:** The week in which the highest number of infectious farms occurred; and **Peak infection:** The total number of farms infected during that peak week.

4.3.8 Sensitivity Analysis

To evaluate the sensitivity of model outcomes to some key parameters in the model, sensitivity analyses were performed for certain DC and D&IC scenarios by creating variations in a single input parameter for each of the three network types of the Model. Scenarios in which epidemics were seeded in farrowing farms (scenarios 1, 4, 7 :DC Scenarios and scenarios 10, 13, 16: D&IC Scenarios) were selected for sensitivity analysis, as these often represented the worst-case scenarios. For the DC scenarios of each network type, we evaluated the impact of altering the network parameters on the outcome of the model: (a) for the scale-free network: the scaling parameter was decreased and increased to 2 and 4 respectively; (b) for the random network: the average connection per farm was increased to 4 to contrast with the baseline model value of 2; (c) and for the small-world network: the average connection per farm was increased to 4 than from baseline model of 2. Additionally, for the small-world network, we evaluated the impact of increasing and decreasing the long-range connection probability to 0.6 and 0.4 respectively. Similarly, to evaluate our assumption regarding indirect contact transmission probabilities, two variations to the baseline D&IC models for each of the three network types were created with modified indirect contact transmission probabilities of 0.05 and 0.25 as compared to the baseline model value of 0.1. For all variations, the outputs were compared based on the proportionate change in median epidemic size as well as the change in die-out percentage, relative to the baseline models.

4.4. Results

The distributions of overall epidemic sizes and the epidemic size by production type, for each of the scenarios, are presented in Figures 4.3 and 4.4 respectively. Descriptive statistics for die-out percentage, total epidemic size, epidemic size for each production type, peak week, and peak infection for each of the 18 simulated scenarios are summarized in Table 4.4. Some fraction of the iterations for most of the scenarios did not result in an epidemic, where the infection died out early due to the stochastic nature of the simulations. The highest stochastic die-out was noticed for scenarios simulated on random networks followed by small-world networks and least for scenarios simulated on scale-free networks. Generally, scenarios with farrowing farms as index herds were more likely to have a smaller proportion of die-out iterations for each of the three network types explored, while scenarios initiated from nursery farms had the highest die-out percentages. The proportion of die-out iterations decreased consistently by around 5-15 percentage points across the three network types and type of index herds when both direct and indirect contact was included in the model. Among the network based models, overall epidemic sizes were largest for simulations based on scale-free networks, while epidemic sizes for random and small-world networks were quantitatively comparable. Similar to the observations regarding stochastic die-out, scenarios with farrowing farms as index herds were more likely to result in larger epidemic sizes than scenarios initiating from other production types. However, for scenarios involving random and small-world networks this effect was less pronounced, where epidemics initiated in any of the three production types resulted in similar epidemic sizes. Nevertheless, with the smallest die-out percentage and with highest

epidemic sizes for most scenarios, epidemics initiating from farrowing farms represented the worst case scenario, and farrowing farms could therefore be characterized as a "super-spreader" class of farm. As nursery and finishing farms, were allowed to recover and revert back to a susceptible status and such farms could have multiple infections, some scenarios resulted in epidemic sizes larger than the total number of farms included in the model.

Not surprisingly, in all three network types explored the DC scenarios resulted in lower overall epidemic sizes than was the case for D&IC scenarios. The impact of including indirect contact into the model was more pronounced for scenarios with random and small-world networks, where the median epidemic size increased by more than 100% (117%-248%) in all the scenarios, and by around 250% for the scenario based on a small-world network where the infection was initiated in farrowing farms. The incorporation of indirect contact into the model, also increased the epidemic size for scenarios based on scale-free networks but only by 20-29%.

No noticeable differences were observed in median time to reach the peak epidemic (peak week) for the three network types, irrespective of the production type from which the epidemic was initiated or whether the scenario included indirect contact. This was largely due to the fact that the median peak week was not reached until the end of the simulation period and the epidemic was still increasing for most of the scenarios. The number of farms infected at the peak week were highest for scenarios based on scale-free networks, while for scenarios with random and small-world networks prevalence of infectious farms at peak week were similar to each other and were much smaller than for

scenarios involving scale-free networks. The number of infected farms at the peak week of infection differed markedly between comparable DC and D&IC scenarios

Variations in parameters associated with each scenario as part of the sensitivity analysis resulted in biologically plausible changes in median epidemic size and die-out percentage values for each of the models evaluated (Table 4.5). The modelled outcomes were most sensitive to an increase in the average number of connections per farm. An increase from 2, in the baseline model, to 4 for direct contact scenarios in both the random and small-world networks, resulted in an approximate increase of 4 to 5 times in the median epidemic size and also to a significant decrease in the proportion of iterations in which die-out occurred. The modelled outcomes were comparatively less sensitive to an increase or decrease in the value of the scaling parameter for direct contact scenarios in the scale-free networks. An increase in the scaling parameter from 3 in the baseline model, to 4 and a decrease to 2, resulted in only a 10% increase and a 20% decrease in the median epidemic sizes respectively. Similarly, modelled outcomes were comparatively less sensitive to changes in the long-range connection probability for direct contact scenarios in the small-world networks. For D&IC scenarios, the influence of altering the indirect contact transmission probability was evaluated. In all three network types it was found that results were sensitive to such changes, though this parameter had the least impact in models based on a scale-free topology.

4.5 Discussion

In this study, we developed and simulated a between-farm PRRS virus spread model by explicitly implementing an empirically-derived contact structure of farm to farm movement of pigs in Canada, in order to evaluate the impact of network structure within

the swine industry on the dynamics of PRRS virus spread. This model is different from previously published models on the spread of PRRS virus (Neumann et al., 2007), as it simulates the spread of PRRS virus through the incorporation of appropriate contact network structures that are typically found to exist among swine farms. Findings from this study provide insights into the importance of incorporating network structure in the modeling of infectious disease spread and thus highlight the value of understanding the contact structures within the population under consideration in any modeling exercise. Furthermore, the methods discussed in this paper can be applied to simulating the spread of other infectious diseases within swine farms via direct and indirect contact as well as to investigate the impact of various network characteristics of a population on disease spread.

As expected, and as discussed in other studies exploring network based models (Moore and Newman, 2000; Pastor-Satorras and Vespignani, 2001; Keeling and Eames, 2005a; Rahmandad and Sterman, 2008; Rahmandad et al., 2011), both network structure and individual heterogeneity had a significant impact on the transmission dynamics of PRRS virus. Scenarios with scale-free networks resulted in the largest epidemic size; scale-free networks have some highly connected farms referred to as "hubs" (Dube et al., 2011) which quickly seeded the infection by infecting its contact farm, therefore infecting maximum farms and with highest prevalence of infected farms at peak week. Once the highly connected nursery and finishing farms have recovered, the transmission in scale-free networks will generally tend to slow down. However, as nursery and finishing farms were allowed to recover in our model, these tended in time to become re-infected and thus led to a further increase in epidemic size. Higher clustering at the local level, in

the topological structure of the network of swine farms, created overlaps in contacts in scenarios based on a small-world network and thus limited the infection in local regions with limited spread to other regions in the network via long-range connections. This resulted in lower epidemic size and lower prevalence at the peak week than was the case for scenarios that adopted scale-free networks. Epidemic size and peak prevalence in scenarios based on random networks were similar to those for small-world networks. This contrasts with what has been observed in other studies, where outbreaks in random networks are reported to have larger or similar epidemic sizes to outbreaks based on scale-free networks (Keeling and Eames, 2005a; Shirley and Rushton, 2005b; Rahmandad and Sterman, 2008; Rahmandad et al., 2011). Random networks are constructed based on equal probability of connection among a subset of farms, which is analogous to assuming a homogenous contact structure. One key fact to help explain the contrast between the findings in this and other studies relates to the difference in average number of connections between farms. In the current study, we set this to be on average two farms, while in a number of other studies this ranged from four up to 10, or even higher (Keeling and Eames, 2005a; Shirley and Rushton, 2005b; Rahmandad and Sterman, 2008; Rahmandad et al., 2011). Studies have shown that the average number of connections is the most important predictor for the epidemic size among other network metrics (Rahmandad et al., 2011; Duncan et al., 2012) and our sensitivity analysis supported this in that an increase in the average number of connections per farm led to much larger epidemic sizes in the random networks.

All sets of scenarios for the network-based models resulted in epidemiologically plausible outcomes. Epidemic size was smaller for scenarios that modelled only direct

contact (DC) when compared to equivalent scenarios that incorporated both D&IC. Incorporation of indirect contact via the sharing of trucks between farms significantly increased the epidemic sizes across all scenarios, highlighting the importance of including this kind of contact in any model addressing the likely spread of the PRRS virus. It also highlights the fact that the swine industry should be vigilant and develop guidelines for proper cleaning and disinfection of vehicles that are shared between farms. Furthermore, it was evident that the impact of including indirect contact was higher for all three network-based models, where this form of contact connected farms that were not directly connected and thus spread infection to otherwise unreachable farms.

The sensitivity of the DC models to a number of network parameters, specifically to the average number of connection per farm in the random and small-world networks, indicated that the likely epidemic size would be much higher as the number of contact farms increased. Similarly, the high level of sensitivity around outcomes in the D&IC models to changes in the indirect contact transmission probability suggests that a better understanding of how to estimate and control this parameter is critical to disease spread. It can be reasonably assumed that this parameter is closely tied to the biosecurity status of farms, and it can be seen that a low transmission probability associated with high biosecurity status (say, ICTP=0.05) will lead to indirect contacts having a limited impact on disease spread when compared to farms with low biosecurity status (ICTP=0.25) where the impact of indirect contacts will be much higher.

ABMs are computationally demanding and may add complexity to the model. The stochastic nature of the simulation also introduces challenges in carrying out sensitivity

analysis. Despite these challenges, such models are increasingly being used as computing resources becomes more widely available and modellers strive to create models that include ever increasing levels of realism (Rahmandad and Sterman, 2008). An ABM, in contrast to a differential equation based model, allows for each object modelled (animal, farm, truck, etc.) to have individual attributes and relaxes the assumption of homogenous mixing among individuals. Nonetheless, the use of simple vs. complex models is an area of on-going debate and there will always be trade-offs in choosing one modelling paradigm over another (Dangerfield et al., 2009). In these models, we only included the transmission of PRRS virus based on direct contacts via the movement of infected animals, and in some we added indirect contact between farms as a result of the sharing of trucks for the movement of animals. We ignored any other mechanisms (aerosol, local spread by fomites, etc.) that may be considered to be involved in PRRS virus spread. We believe, for farm-to-farm transmission of the virus, that the movement of infected pigs is the most important mechanism. Aerosol transmission and local spread of PRRS virus is considered to be limited within the geographical area of an infected farm (Mortensen et al., 2002; Holtkamp et al., 2010) and thus would have at most a limited role in long-range transmission. However, the current model can further be expanded to incorporate spatial location of farms that would allow to local area spread of the virus and will be helpful in evaluating the impact of this mode of transmission. Other forms of indirect contacts between farms were ignored, first due to unavailability of data to parametrize any such contacts and second due to the likely impact of such contact eg. sharing of personnel, equipments etc. were

considered to be localized within close proximity of the farms and may not influence transmission of the virus over long-ranges.

We encourage readers not to make strong quantitative inferences from the findings of this study regarding PRRS virus spread. Inevitably, it has not been possible to incorporate all relevant factors governing disease spread in these models and some uncertainties associated with parameter estimates will exist in any model (Garnett, 2002). One of the limitations in the current study was that the AnyLogic software did not allow for the small-world networks to reflect the precise characteristics of the observed network of swine farms. Second, for network based models, we used static links between farms for each iteration, while in reality connection preferences among farms may change over time. The network models also assign the same weight to each connection, while in practice the strength of connections can vary as the shipments between pairs of farms may involve variable number of animals. Studies have demonstrated that outputs can differ when dynamic connections (Vernon and Keeling, 2009) or connections with variable weighting (Rahmandad and Sterman, 2008) are incorporated in network models. In the current models, we allowed finishing farms to ship animals to farrowing farms. However, in reality farrowing farms may not always receive replacement animals from finishing farms, or may do so from only a subset of finishing farms as well as from more specialized breeding farms. Such replacement stocking was not represented in the model, as no relevant contact data for such transfers was available. We speculate that allowing the movement of animals from finishing to farrowing farms might have resulted in comparatively larger epidemic sizes when the virus was seeded in finishing farms than when it was shed in nursery farms. Typically,

such stock replacement oriented farms would be expected to maintain higher levels of health and biosecurity, so that the extent of spread of PRRS virus to farrowing farms via direct contact may be more limited than what was modelled in this study.

We used estimated rates of truck sharing between different production types to represent the indirect contact between farms. Studies have shown that the trucks themselves can act as an epidemiological unit where animals from different farms can spread the virus or can transmit the virus mechanically (Dee et al., 2002c; Dee et al., 2004b). Network study analysing truck sharing between farms have shown that truck sharing patterns typically follow a power-law distribution (Thakur et al., 2014), implying that the network of farms and trucks will exhibit a scale-free topology. Given these factors, representing trucks as a separate agent class and allowing them to follow an independent clean-infected-clean cycle with appropriate connection into the farm networks, may have imparted greater realism to the model though at the expense of added complexity.

4.6. Conclusion

The current study has demonstrated noticeable differences on the extent of spread of PRRS virus when a number of network structures among the swine herds are considered, which highlights the importance of understanding and incorporating realistic contact structures among the individuals of a population while developing infectious disease spread models. The study further revealed that irrespective of the types of network structures explored, indirect contact significantly played role in further spreading the infection to individuals in the population, which were not directly connected. Finally, it should be noted that we used characteristics of real contact structures of swine movement networks to simulate network structure in a hypothetical

swine population on which PRRS virus spread was explored; however, simulating the spread of the virus on actual farm to farm movement data may provide realistic model outcomes and which may differ to some extent from the findings in this study.

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Table 4.1 Study population and transmission parameters used for simulation of network based models of PRRS virus spread

Parameters	Value	Reference
Total Farms (N)	**500**	assumed
Farrowing farms	100 (20%)	
Nursery farms	150 (30%)	
Finishing farms	250 (50%)	
Transmission Probability	1 (direct contact)*	(Neumann et al., 2007)
	0.1 (indirect contact)*	assumed
Infectious Duration (week)		
Farrowing farms	Whole duration of simulation	(Neumann et al., 2007)
Nursery Farms	4.5 weeks	(duration of stay)
Finishing Farms	Uniform(12,15) weeks	(duration of stay)
Network Parameters		
Connection/farm	2	(Thakur et al., 2014)
Scaling Parameter	3	(Thakur et al., 2014)
Probability of long-range connection	0.5	assumed [a]

*for all production types

[a]The value for probability of long-range connection was set as to closely reflect the clustering coefficient of the network to that observed in swine movement network in Canada (Thakur et al., 2014).

Table 4.2 Description of direct and indirect contact rates used for simulation of network based models of PRRS virus spread

Contact Groups	Mean Contact rate/week	
	Direct	Indirect
Farrowing-Nursery	0.51	0.04
Farrowing-Finishing	0.03	0.006
Farrowing-Farrowing	0.01	0.11
Nursery-Nursery	-	0.1
Nursery-Finishing	0.31	0.165
Nursery-Farrowing	-	0.04
Finishing-Nursery	-	0.165
Finishing-Finishing	-	0.55
Finishing-Farrowing	0.25	0.006

The contact rates were obtained from a pig movement traceability study (Thakur et al., 2014) except for direct contact between Finishing-Farrowing, which was based on our assumption that a proportion of farrowing farms will replace gilts from finishing farms at approximately the rate noted.

Table 4.3 Description of scenarios for simulation of network based model of PRRS virus spread

Scenario Number	Scenario Name	Network Type/ Model	Initially infected production type	Spread by Direct Contact[a]	Spread by Indirect Contact[b]	Transmission Probability	
						Direct Contact	Indirect Contact
1	SF_DC_F	Scale-free	Farrowing	Yes	No	1	NA
2	SF_DC_N		Nursery				
3	SF_DC_Fi		Finishing				
4	RAN_DC_F	Random	Farrowing				
5	RAN_DC_N		Nursery				
6	RAN_DC_Fi		Finishing				
7	SW_DC_F	Small-world	Farrowing				
8	SW_DC_N		Nursery				
9	SW_DC_Fi		Finishing				
10	SF_D&IC_F	Scale-free	Farrowing		Yes		0.1
11	SF_D&IC_N		Nursery				
12	SF_D&IC_Fi		Finishing				
13	RAN_D&IC_F	Random	Farrowing				
14	RAN_D&IC_N		Nursery				
15	RAN_D&IC_Fi		Finishing				
16	SW_D&IC_F	Small-world	Farrowing				
17	SW_D&IC_N		Nursery				
18	SW_D&IC_Fi		Finishing				

[a]spread of disease from one farm to another through movement of infected pigs

[b]spread of disease from one farm to another through sharing of trucks

SF=Scale-free, RAN=Random, SW=Small-world, DC=Direct Contact, D&IC=Direct and indirect contact, F=Farrowing, N=Nursery, Fi=Finishing,

Table 4.4 Descriptive summaries of die-out percentage, epidemic size, time required to reach the peak epidemic and the number of farms infectious at peak week obtained from 500 iterations of each of 18 scenarios of simulated outbreaks of PRRS virus considering three contact network structure of swine herds

Scenario	Die-out Percentage	Median Epidemic Size (p5-p95)				Peak Weak	Peak Infection
		Total	Farrowing	Nursery*	Finishing*		
Direct Contact Scenarios							
1. SF_DC_F	0	613 (449-717)	96 (92-100)	242(163-293)	274 (189-330)	50	233
2. SF_DC_N	89.6	443 (96-640)	93 (30-99)	124 (32-256)	199 (34-289)	52	211
3. SF_DC_Fi	45.2	550 (269-679)	96 (74-100)	209 (87-271)	244 (107-304)	51	228
4. RAN_DC_F	16.6	34 (6-103)	5 (1-18)	10 (0-31)	19 (0-54)	51	19
5. RAN_DC_N	87.8	36 (13-85)	6 (1-16)	10 (4-24)	24 (6-53)	51	16
6. RAN_DC_Fi	56.4	47 (8-102)	7 (1-20)	11 (0-29)	29 (4-57)	51	21
7. SW_DC_F	10.6	31 (6-111)	7 (1-16)	11(0-34)	15 (2-59)	51	16
8. SW_DC_N	86.6	41 (10-109)	6 (1-18)	11 (1-30)	22 (5-60)	51	18
9. SW_DC_Fi	66.4	43 (7-115)	7 (1-20)	10(0-30)	23 (15-65)	51	20

p5/p95 -5th and 95th percentile of the distribution of epidemic size

*median epidemic sizes for infected nursery and finishing farms are larger than the total population of these farms included in the model, which is due to reinfection of some of these farms and summary statistics of reinfected farms is presented in table 5.

Summary statistics for all model scenarios excluded iterations with stochastic die-out (iterations resulting in epidemic size less than

Table 4.4 (Continued)

Scenario	Die-out Percentage	Median Epidemic Size (p5-p95)				Peak Weak	Peak Infection
		Total	Farrowing	Nursery*	Finishing*		
Direct and Indirect Contact Scenarios							
10. SF_D&IC_F	0	747 (588-850)	98 (94-100)	298 (218-354)	347 (263-405)	50	264
11. SF_D&IC_N	83	569 (8-775)	94 (1-100)	214 (6-307)	256 (4-373)	51	249
12. SF_D&IC_Fi	37	660 (335-824)	97 (81-100)	256 (109-341)	306 (139-392)	51	255
13. RAN_D&IC_F	11.4	92 (11-211)	11 (1-29)	27 (4-65)	53 (4-119)	51	39
14. RAN_D&IC_N	76.4	86 (6-189)	12 (0-28)	26 (2-54)	50 (3-112)	51	38
15. RAN_D&IC_Fi	45.8	102 (9-213)	13 (2-30)	30 (2-66)	60 (6-122)	51	43
16. SW_D&IC_F	3.8	108 (14-259)	15 (1-37)	31 (4-81)	60 (6-145)	51	48
17. SW_D&IC_N	75.6	89 (7-251)	12 (0-35)	23 (2-75)	49 (5-136)	51	39
18. SW_D&IC_Fi	51.6	103 (10-258)	14 (1-35)	28 (12-78)	60 (7-143)	51	48

p5/p95 -5th and 95th percentile of the distribution of epidemic size

*median epidemic sizes for infected nursery and finishing farms are larger than the total population of these farms included in the model, which is due to reinfection of some of these farms and summary statistics of reinfected farms is presented in table 5.

Summary statistics for all model scenarios excluded iterations with stochastic die-out (iterations resulting in epidemic size less than

Table 4.5 Sensitivity analysis as it affected median epidemic size and die-out percentage values in simulated PRRS virus outbreaks within the various network based models assuming direct and indirect contact

Scenarios	Parameters				Median epidemic size (p5-p95)	% ± in median outcome	Die out Percentage
	M	ICTP[a]	CPF[b]	LRCP[c]			
Direct Contact Scenarios							
1. SF_DC_F	**3**	**-**	**-**	**-**	**613 (449-717)**	**-**	**0**
SF_DC-F with change in scaling parameter to 2	2	-	-	-	488 (326-596)	-20	0
SF_DC-F with change in scaling parameter to 4	4	-	-	-	671 (490-795)	10	0
4. R_DC_F	**-**	**-**	**2**	**-**	**34 (6-103)**	**-**	**16.6**
R_DC_F with change in connection per farm to 4	-	-	4	-	159 (32-311)	368	2.4
7. SW_DC_F	-	**-**	**2**	**0.5**	**31 (6-111)**	**-**	**10.6**
SW_DC_F with change in connection per agent to 4	-	-	4	0.5	189 (21-392)	510	0.6
SW_DC_F with change in long-range connection probability to 0.4	-	-	2	0.4	27 (7-101)	-13	9.6
SW_DC_F with change in long-range connection probability to 0.6	-	-	2	0.6	32 (7- 117)	3	8
Direct and Indirect Contact Scenarios							
13. SF_D&IC_F	**2**	**0.1**	**-**	**-**	**747 (588-850)**	**-**	**0**
SF_D&IC_F with change in ICTP to 0.05	2	0.05	-	-	674 (516-780)	-10	0
SF_D&IC_F with change in ICTP to 0.25	2	0.25	-		940 (764-1056)	26	0
16. R_D&IC_F	**-**	**0.1**	**2**	**-**	**92 (11-211)**	**-**	**11.4**
R_D&IC_F with change in ICTP to 0.05	-	0.05	2	-	62 (7-134)	-33	15
R_D&IC_F with change in ICTP to 0.25	-	0.25	2	-	324 (21-556)	252	5.8
19. SW_D&IC_F	**-**	**0.1**	**2**	**0.5**	**108 (14-259)**	**-**	**3.8**
SW_D&IC_F with change in ICTP to 0.05	-	0.05	2	0.5	54 (11-169)	-50	6.6
SW_D&IC_F with change in ICTP to 0.25	-	0.25	2	0.5	409 (44-653)	279	1.4

[a]Indirect Contact Transmission Probability, [b]Connection Per Farm, [c]Long Range Connection Probability, p5-p95=-5th and 95th percentile of the distribution of epidemic size

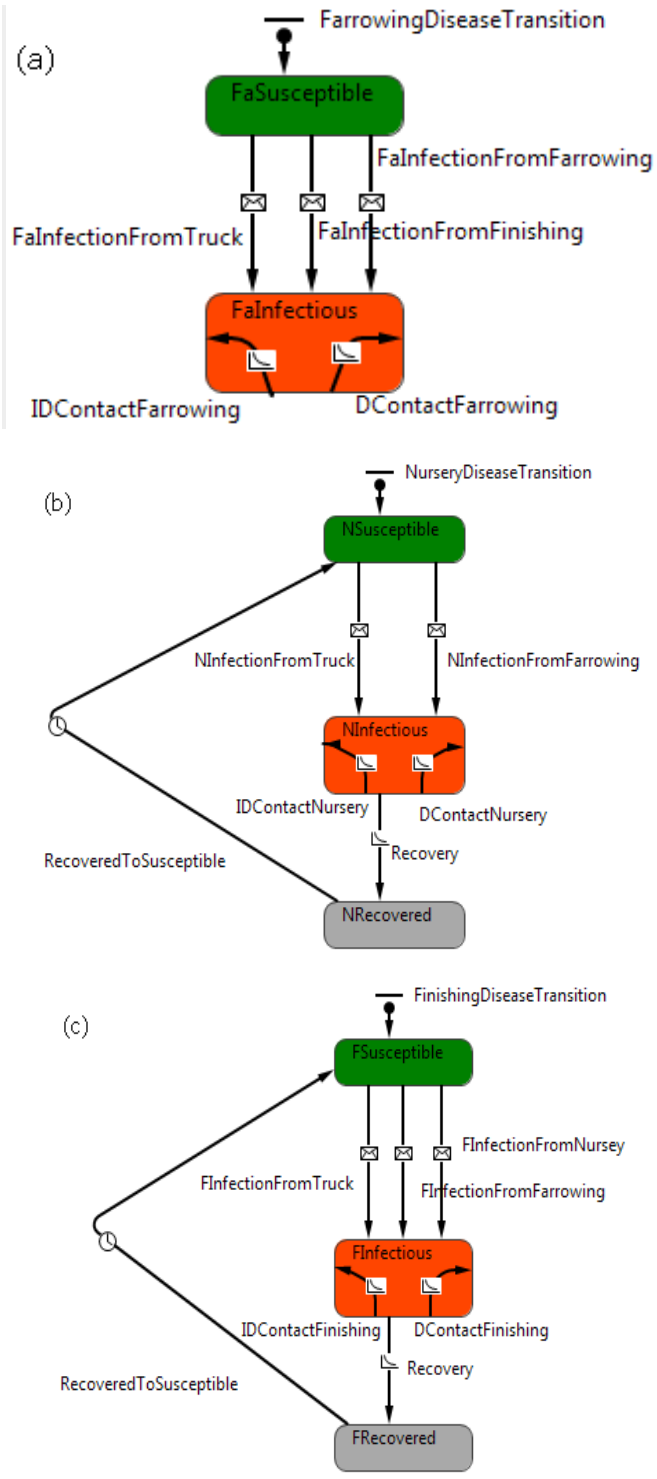

Figure 4.1 Transition of PRRS virus infection for swine herds from susceptible to infectious (SI) for farrowing farms (a) and from susceptible to infectious to recovered to susceptible (SIRS) for the two other production types (b and c), DContact is contact via movement of animals between farms and IDContact is contact between farms due to sharing of trucks.

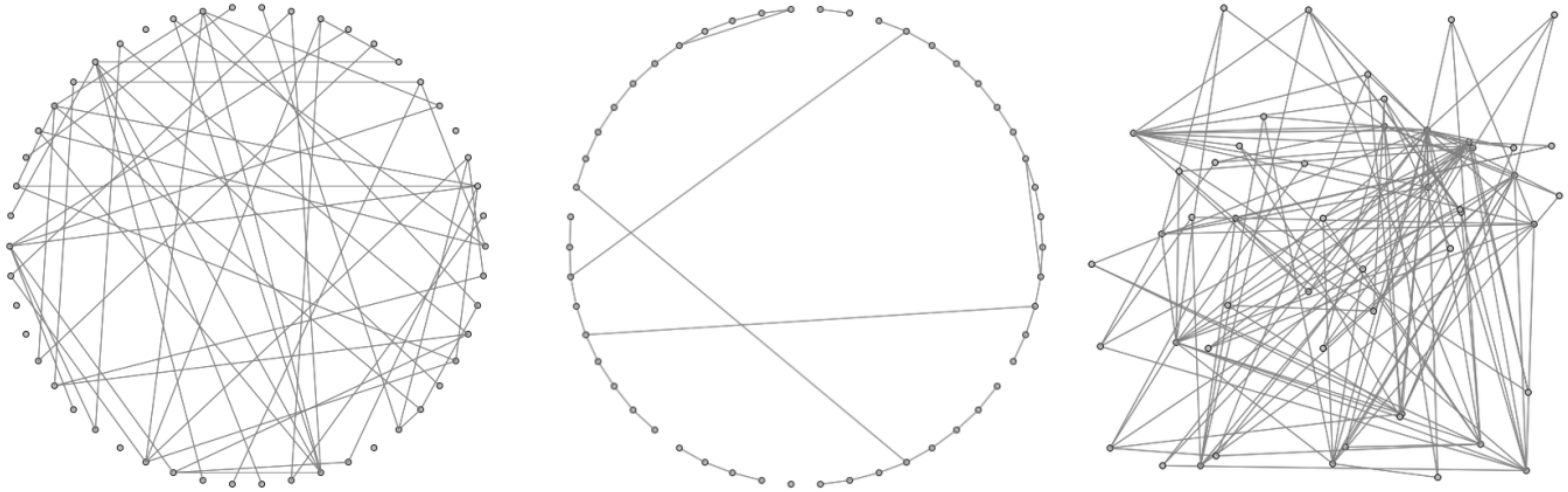

Figure 4.2 Example of three distinct network types, each containing 50 nodes. From left to right: Random (with two connections per node), Small-world (with two connections per node and neighbor link probability of 0.95) and Scale-free (with scaling parameter M=3); generated using AnyLogic 7.02.

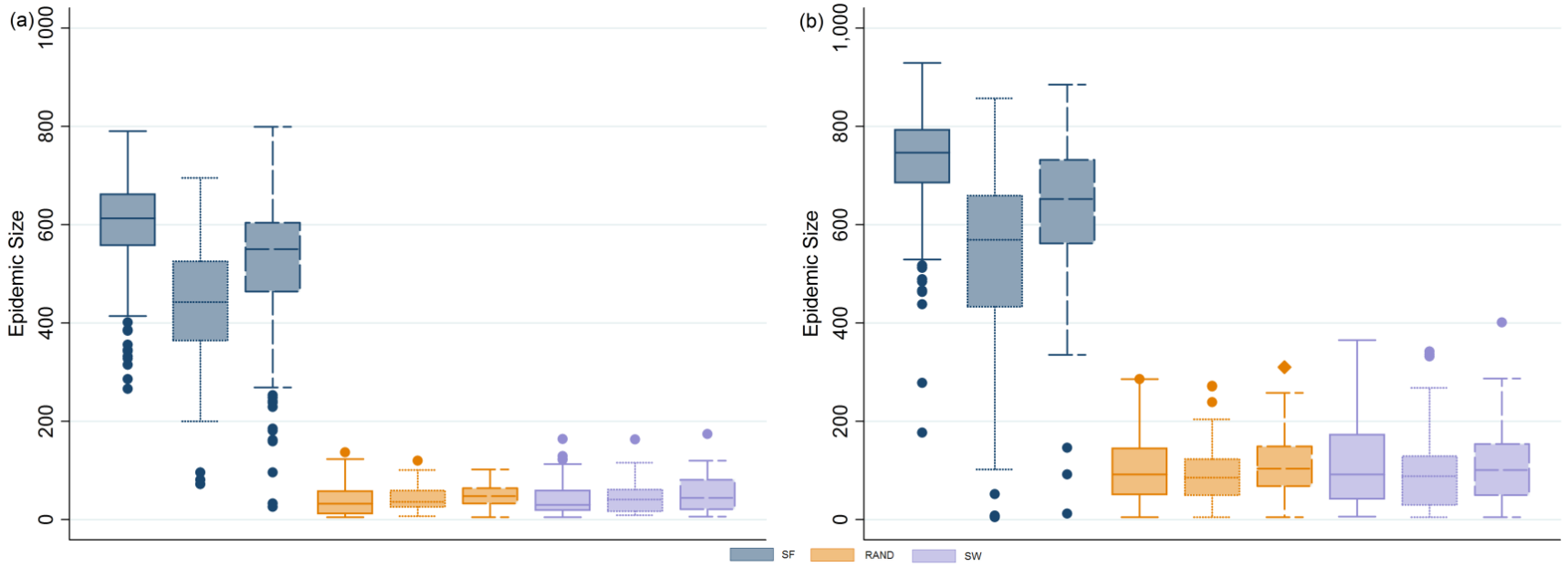

Figure 4.3 The distribution of the overall epidemic size of PRRS virus outbreaks obtained from simulations of between-farm spread of PRRS virus in a virtual population of 500 swine herds considering three different contact network structure among swine herds under assumptions of (a) direct and (b) direct and indirect contact between farms. Different colors represent scenarios for each of the three network types. Boxes with solid lines, tight dots and long dash represent epidemics initiated from farrowing farms, nursery farms and finishing farms respectively.

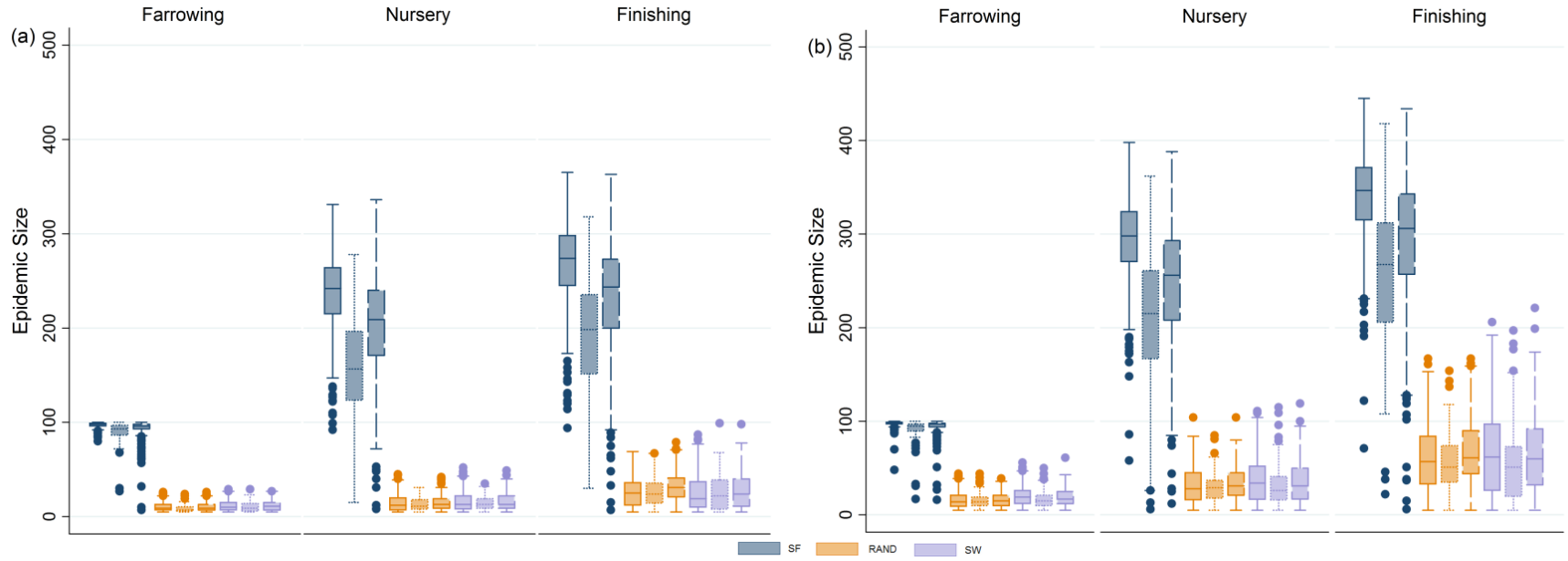

Figure 4.4 The distribution of epidemic size of PRRS virus outbreaks by production type of swine herds obtained from simulations of between-farm spread of PRRS virus in a virtual population of 500 swine herds considering three different contact network structure among swine herds under assumptions of (a) direct and (b) direct and indirect contact between farms. Different colors represent scenarios for each of the three network types. Boxes with solid lines, tight dots and long dash represent epidemics initiated from farrowing farms, nursery farms and finishing farms respectively.

Chapter 5 Bayesian analysis for modelling contamination of trucks used in the shipment of pigs infected with porcine reproductive and respiratory syndrome virus

5.1 Abstract

Porcine reproductive and respiratory syndrome (PRRS) is a major disease in the swine industry. PRRS virus is primarily transmitted by direct and indirect contact between farms and through aerosol. Recent studies have suggested an increasing degree of truck sharing used for the shipment of pigs between farms. Other studies have highlighted the importance of trucks in the spread of PRRS virus. In the present analysis, a Bayesian approach was applied to quantify the likelihood that a shared truck used in the shipment of pigs would be infected with PRRS virus at the end of a given day, and to evaluate the efficacy of cleaning and washing protocols in reducing virus transmission during shipment. PRRS virus-infected farms from which trucks shipped pigs were deemed to be the source of infection. A quantitative stochastic model was built using data related to the prevalence of PRRS virus-positive herds, number of times a truck is typically shared on any given day, shipment size, animal-level PRRS prevalence and virus shedding, travel time between farms, and the efficacy of three different cleaning and disinfection procedures. The model resulted in a mean probability of 0.394 that a truck would be infected at the end of a day when that truck had been used by a finishing farm, without considering the number of previous uses of the truck or whether or not it had been washed and disinfected. The action of washing trucks on its own resulted in a negligible decrease (less than 5%) in the probability that a truck would be infective; washing and disinfection resulted in a moderate decrease (approximately 58%), while washing and disinfection, followed by drying, had the highest impact with a greater than 90% reduction in the probability. Findings from this study suggest that under current biosecurity practices, where only around one third of trucks are completely cleaned and

disinfected between successive shipments, and where for more than half of the shipments made on any given day the same truck is used by more than one farm, a substantial risk exists for the spread of PRRS virus as a consequence of sharing trucks.

5.2 Introduction

Porcine reproductive and respiratory syndrome (PRRS) is a major viral disease of swine with devastating economic consequences to the swine industry (Neumann et al., 2005). All ages of pigs are susceptible to PRRS virus, with highly variable clinical manifestations in different age groups of infected pigs ranging from abortion, anorexia and pyrexia in pregnant sows to respiratory symptoms, high mortality and poor growth in young pigs (Nodelijk, 2002). Several direct and indirect mechanisms have been identified for the spread of PRRS virus from one farm to another. The direct contact routes include the movement of infected animals and the use of contaminated semen, while the indirect mechanisms involve fomites (Yaeger et al., 1993; Mortensen et al., 2002; Otake et al., 2002c), and the sharing of equipment and shipment trucks between farms (Otake et al., 2002b; Dee et al., 2004b). Transmission via aerosol has also been reported (Otake et al., 2002a; Otake et al., 2010). Additionally, some studies have implicated the role of insects such as mosquitoes and house flies in mechanical transmission of the virus (Otake et al., 2002d; Otake et al., 2003).

The movement of animals or the sharing of equipment, personnel, etc., through which susceptible animals are brought into direct or indirect contact with infected animals, can be instrumental in spreading infectious agents between farms (Ortiz-Pelaez et al., 2006). In recent years network analysis has elucidated contact patterns among animal holdings

in specific livestock industries (Dubé et al. 2008; Smith et al. 2012). In a number of recent swine movement analysis studies in Denmark and France, the importance of transportation vehicles as a means to spread infectious agents among farms that are otherwise not directly connected has been identified (Bigras-Poulin et al., 2007; Rautureau et al., 2012a; Smith et al., 2012). In our recent study that characterized swine movement in four Canadian regions (Thakur et al., 2014), we identified similar patterns of truck sharing between farms to those described in the UK (Smith et al., 2012), France (Rautureau et al., 2012a) and Denmark (Bigras-Poulin et al., 2007), with one truck on average being shared between four different farms. Similarly, for more than 50% of all shipments on any particular day, the same truck had been used in at least one additional shipment. As the same vehicles were used multiple times and were shared by different farms for the shipment of pigs, they connected farms which would otherwise have no direct contact. Thus any inadequate cleaning and disinfection of vehicles is likely to increase the risk of infectious agents being spread, as has been implicated in the recent spread of Porcine Epidemic Diarrhoea (PED) virus across North America (Lowe, 2014). Additionally, these vehicles can spread infectious agents mechanically or indirectly via contaminated fomites (faeces, bedding material, etc.) (Alexandersen et al., 2003).

The role of transportation vehicles in the spread of PRRS virus to susceptible pigs has been demonstrated through experimental studies. Sentinel pigs became infected after being housed in an artificially contaminated trailer and in trailers which housed experimentally infected pig before the introduction of the sentinel pig (Dee et al., 2004b). Similarly, mechanical transmission of PRRS virus via transportation during cold and warm weather (with limited frequency) has been documented by the same

authors (Dee et al., 2002a; Dee et al., 2003). In these experiments, Dee and colleagues also evaluated cleaning and disinfection protocols. PRRS virus from the trailers was detected in all combination of cleaning and disinfection treatments, except when bedding removal, washing, disinfecting and drying were combined (Dee et al. 2004a). In a similar study to assess the sanitation protocols of commercial transport vehicles contaminated with PRRS virus, it was demonstrated that washing and fumigation with glutaraldehyde-quaternary ammonium chloride or washing and disinfection plus overnight drying, were the most effective treatments (Dee et al., 2004a). One recent study has suggested the relative importance of truck sharing in the spread of one particular genotype of PRRS virus among swine herds in Ontario (Kwong et al., 2013).

The swine industry in North America has become increasingly specialized and integrated, with the adoption of three-site production systems which requires regular movement of pigs between sites (Key and McBride, 2010). Canadian swine producers and experts in the swine industry have been concerned about the role of shared trucks on farm to farm spread of PRRS virus (http://www.opic.on.ca/biosecurity-resources/transportation). The objectives of the analyses described here were to quantify the likelihood that a truck used for the shipment of pigs would be infected with PRRS virus at the end of any given day (as well as on subsequent days), and to evaluate the efficacy of cleaning and disinfection protocols in eliminating the virus from these trucks using a Bayesian approach. The model estimates the probability that a truck will be infected with PRRS virus after it has been used by a number of farms on any given day and also provides estimates on the likelihood that the truck will still be infective on subsequent days. Additionally it provides insights into the likelihood that the PRRS

virus will be eliminated from the trucks after cleaning and disinfection protocols have been applied.

5.3 Material and Methods

A Bayesian approach was selected for this study as it allows for the combination of different sources of information and the propagation of uncertainty in the model (Czado and Brechmann, 2014). It also allows the assumption of conditional dependence between nodes required by classical risk assessment to be relaxed, supporting the estimation of joint probability distributions at nodes that are conditionally independent, through the use of Bayesian networks (Albert et al., 2008).

A schematic diagram of truck use, informed by a pilot pig traceability data in Canada (Thakur et al., 2014), is illustrated in Figure 5.1. A given truck may be used by two or more farms on any given day and may or may not be cleaned between successive shipments. A schematic representation of the Bayesian model is presented in Figure 5.2. The baseline model estimates the probability that a truck "i" is infected with PRRS virus at the end of Day 1, given it visited "j" farms on that day and that at least one of those farms was infected with PRRS virus. It additionally considers whether the truck had sufficient viral load to make it infective, which is determined by the travel time of the truck during the shipment, the size of the shipment, the animal level prevalence and the probability of there being shedding animals in the batch of animals shipped. The probability of shedding animals further depended on the production type "k" of the infected farm. The baseline model further incorporated one of the three cleaning and disinfection protocols "l" and evaluated the efficacy of these protocols in eliminating the

PRRS virus from contaminated trucks. This risk assessment considered the following nodes as influencing the probability that a truck would be contaminated with PRRS virus at the end of that day's work: 1) farm-level prevalence of PRRS virus, 2) number of farms using the same truck on any given day, 3) number of animals shipped on the truck, 4) animal-level prevalence of PRRS virus in the group of shipped pigs, 5) proportion of animals shedding the virus in the group - which in turn depends on the stage of growth of the pigs being shipped and the time of travel between two farms. A detailed description of the nodes is presented in Table 5.1, with a summary of the underlying assumptions and associated input values. In the absence of any prior knowledge we use non-informative prior distributions. Finally, we estimated the probability that a truck "i" would be infected with PRRS virus by multiplying the probability that at least one of the farms "j" that it had visited was infected with PRRS virus, the probability that the truck had more animals in that shipment than $Min_{ani.k}$ and the probability that the travel time was more than two hours.

Simulated Models

Three sets of models were evaluated to estimate the likelihood that the trucks shared between farms for shipment of pigs were contaminated with PRRS virus. First a baseline model was simulated without any cleaning or disinfection protocols applied to the truck, which resulted in an estimation of the probability that the truck would be contaminated at the end of Day 1. The baseline model was then extended to incorporate decay of the virus over time for two different seasons, warmer months (when the ambient temperature is around 22^0C) and colder months (when the ambient temperature is around 4^0C or less), to assess the probability that the truck would remain contaminated

on subsequent days under these conditions. Finally, the baseline model was further developed to evaluate the efficacy of commonly used cleaning and disinfection protocols in eliminating the virus from trucks.

Data Description

Data used for this study were obtained from the literature (Dee et al., 2004a; Dee et al., 2004b; Thakur et al., 2014) and from pilot pig traceability data from four Canadian regions described elsewhere (Thakur et al., 2014).

For this study, we assumed that a truck was free of PRRS virus when it was used for the first time on Day 1. Further, in order to assess the perpetuation of the risk on Day 2 and subsequent days, we did not consider any new sources of infection for that truck, so that all farms visited by the truck after the first day were assumed to be clean. Based on experts' judgement, we assumed the farm-level prevalence of PRRS virus to be 50% (F.Prev). Two supervisory commiittee members for this thesis research (DH, a Professor of swine health management, and ZP, an Associate Professor of Veterinary Epidemiology), who have extensive expertise in swine production and management across Canada provided inputs to estimate some of the assumed parameter values. Based on the F.Prev of the virus, number of farms that could be infected with PRRS virus out of the farms visited by the truck on any day and the probability that at least one of the visited farms was infected with PRRS virus was estimated.

Truck use

The proportion of trucks used ($Tr.use_i$) for two, three and four or more “j” farm visits on a given day and the proportion of trucks with more than the minimum number of

shipped animals (Min_{ani}) for each of three "k" production types were obtained from the pilot pig traceability data.

Shipment size and travel time

The number of infectious animals in a given shipment, and the travel time were estimated as described below:

Prevalence of shedding animals on a truck

The prevalence of shedding animals (Shed.prev.k) was adjusted by the within-farm prevalence of PRRS ($A.Prev._k$). Expert judgement suggested that the proportion of animals shedding the virus ($Shed.anim._k$) varied according to the growth stage of the pigs being transported and it was suggested that 20%, 50% and 70% of weaned piglets, nursery pigs, and finishing pigs, respectively, would typically be shedding the virus.. Several studies have reported very high within-farm prevalence of PRRS virus ranging from 80 -100% (Dee and Joo, 1994; Maes, 1997; Nodelijk et al., 2003). For this study, we used an animal-level prevalence ($A.Prev._k$) of 80% and evaluated the impact of this variable on the model outcome by carrying out sensitivity analysis.

Minimum number of shedding animals in a shipment

PRRS virus is excreted through urine, faeces and oral fluids of infected animals in addition to several other bodily secretions (Wills et al., 1997c; Bierk et al., 2001), though the dynamics of these shedding patterns is not well documented. Therefore, it was difficult to quantify the amount of PRRS virus likely to be present on any given shipment truck. We were interested in estimating the infectious potential of the trucks such that the virus could be transmitted to naive animals. We therefore assessed whether or not the trucks would likely have sufficient viral load to infect susceptible pigs. Dee

and colleagues (2004b) demonstrated that the presence of two infectious pigs on a truck trailer for two hours was sufficient to transmit the virus to naive pigs on the subsequent introduction of these animals to the truck. Using these guidelines as a cut-off value, we categorized trucks as having sufficient infectious virus or not to transmit PRRS virus to naïve pigs (i.e. they must have transported at least two infectious animals and have had a travel time of at least two hours).

Minimum number of animals ($Min_{ani.k}$) on a truck to have at least two infectious animals

We used the hypergeometric distribution to estimate the minimum number of shedding animals needed in a shipment ($Min_{ani.k}$) for each production type, in order to have two infectious animals (Nani) on a truck that were shedding the virus. We used the maximum number of shipped animals ($Ship_{size.k}$), as recorded in the pilot pig traceability data, for each of the three production types as 'N', and the number of shedding animals, which was based on Shed.prev.k, as the 'm' parameter of the hypergeometric process. For psi, we used one, as the odds of drawing a shedding animal from the shipment was similar to that of drawing an animal that was not shedding the virus.

Shipment size ($Ship_{size}$) and Minimum shipment size ($Min_{ship.k}$)

The shipment size was simulated as a uniform distribution with minimum and maximum number of animals as recorded in the pilot pig traceability dataset for each of the three production types. Based on this distribution for shipment size, the probability that a truck had minimum shipment size ($Min_{ship.k}$) or more animals than $Min_{ani.k}$ was estimated using the step function available in OpenBUGS.

Infective Dose (Inf.dose)

Finally, we estimated the probability that a truck has an infective dose of PRRS virus (Inf.dose) if it shipped at least Min_{ani} and had a travel time (Travel) of at least two hours.

Additionally, since the infectious dose is related to the environmental conditions, we calculated the infective dose (Inf.dose) for warm and cold seasons. PRRS virus has been described as having a median infectious half-life of 14.6 hours (95% CI = 12.6 - 17.2) in pig manure at an ambient temperature of 22^0 C (Linhares et al., 2012). The PRRS virus has a comparatively longer half-life of 112.6 hours (95% CI = 103.2 - 123.8) in pig manure at an ambient temperature of 4^0 C (Linhares et al., 2012). We were guided by this information to extend the model to incorporate viral decay in order to quantify the risk that trucks would still be contaminated with PRRS virus on subsequent days in either warm and cold months.

For warmer months, we assumed that at least one infectious dose of virus would be present on trucks that have at least two infectious animals, that had been kept on the truck for at least two hours. So, based on viral decay with an assumed half-life of 15 hours, for at least one infectious dose of virus to be present during the 15 hours subsequent to the truck being used on Day 1, would require that at least four infectious animals (this is analogous to having two infectious doses of virus on Day 1) were present on the truck, and similarly for the truck to be infectious for the next 30 hours that at least eight infectious animals would need to have been present. On the other hand, for colder months we assumed that trucks with at least two infected animals could be considered to be infective for around five days, as the half-life of the virus is much

longer (112.6 hrs at 4^0C), and thus we did not attempt to quantify the likelihood for time points beyond a one week duration from which the truck initially became infected.

Travel time

In order to estimate the amount of virus shed during transportation, the travel time was first estimated and then the probability that a given shipment was longer than two or more hours was computed. It was assumed that the most likely travel time in Ontario, Canada was around two hours, which corresponds to the travel time estimated by Dee et al. (2004b) for swine operations in Minnesota and was likely to vary between a minimum of half an hour and a maximum of six hours. We used this information to parameterise a normal (mean, precision) distribution in OpenBUGS. First, the mean was computed as (min+2*mode+max)/6, and the precision was computed as 1/((max-min)/6)^2. The obtained distribution was further truncated to avoid travel time values below zero. These equations provided a normal (2.43, 1.22) distribution for the travel time parameter.

The probability that a given shipment lasted for at least two hours was estimated using the step function to the distribution of travel time. The step function, provided the probability of travel time equal to 1 if the travel time was more than two hours.

Evaluation of cleaning and disinfection protocols

The baseline model was then extended by including three cleaning and disinfection protocols identified to eliminate the PRRS virus from contaminated trucks. Trucks infected with PRRS virus require rigorous cleaning, disinfection and drying to eliminate the virus (Dee et al., 2004a; Dee et al., 2004b). The Canadian Swine Health Board has developed protocols to wash, disinfect and dry such transport vehicles

(http://www.swinehealth.ca/publications.php). However, from anecdotal evidence there appears to be a lack of consistency in the application of these standard protocols, with some trucks being cleaned only by washing, while in other cases washing is followed by disinfection, and for some washing, disinfection and overnight drying is practiced. In experimental studies, Dee and colleagues (Dee et al., 2004a; Dee et al., 2004b), evaluated the efficacy of each of these protocols (washing, washing with disinfection, and washing with disinfection followed by drying for 12 hours). We used data from those studies (as summarised in Table 5.1) for each of the three cleaning protocols, to assess their effectiveness in reducing the probability that a truck used for shipment of pigs would remain contaminated with PRRS virus .

Scenarios

A total of 21 scenarios were constructed and analysed (Table 5.2). A subset of 12 of those scenarios did not include any cleaning and disinfection control measures, while the other nine scenarios evaluated the efficacy of each of the three cleaning and disinfection protocols. For scenarios without cleaning and disinfection protocols, we evaluated the risk for trucks used by two, three, or four or more farms, and also estimated the combined risk for a random truck for which the number of farms previously visited on that day was unknown. Additionally, the production type of the initial infected farm on which the truck was used was also included in these scenarios. Similarly, for scenarios with cleaning and disinfection protocols, we estimated the risk that a random truck would be used by any of the three production types and would be cleaned by the application of one of the three cleaning protocols.

Stochastic model

To quantify the probability that a truck used by a number of farms on a given day would be infected with PRRS virus at the end of the day, a stochastic model was developed in OpenBUGS 3.2.2 (Lunn et al., 2009). A total of 60,000 iterations with a burn-in period of 3,000 were obtained after initializing the model with three chains. The convergence, diagnostic analyses and summary of all posterior distributions were computed in R using the CODA package (Plummer et al., 2006). The convergence of the MCMC model was assessed both visually using the history and autocorrelation plots, and formally using the Brooks-Gelman-Rubin diagnostic (Gelman and Rubin, 1992), which provided an estimate of the shrinkage or scale reduction factor for each of the nodes and scenarios. The distribution of the scale reduction factors (median and 97.5% upper bounds) were plotted to visually assess convergence. Once, the model converged, the effective sample size was estimated by running the model for sufficient number of iterations till the MCMC error became less than 5% of the posterior standard deviation for monitored nodes. The mean, for the scenarios described above, median, and 95% CrI (credible interval) for each stochastic node are reported.

Sensitivity Analysis

A sensitivity analysis was performed for one scenario (S.4.fi), where the truck was used by four or more farms, carried finishing pigs, and without application of any cleaning and disinfection measures. The aim was to evaluate and identify what-if scenarios that could lead to significant decrease or increase in the final probability. We evaluated the percentage change in the mean probability of infection compared to the original scenario. We assessed these changes using farm-level prevalence (F.Prev) of PRRS of

10%, 30% and 70%, animal-level prevalence (A.Prev) of 10%, 30%, 50%, and 100%, and animal shedding proportions (Shed.ani) of 10%, 30% 50% and 90%. Additionally, we evaluated the sensitivity of the model by changing Nani to 4 and 8.

5.4 Results

The mean probabilities of a truck remaining contaminated with PRRS virus at the end of Day 1, for scenarios without and with the application of various cleaning and disinfection measures are presented in Figure 5.3. Similarly, the mean, median and 95% CrI for all the parameters used in the model and for all the scenarios are summarised in Appendix, Table S9 and their density plots are presented in Appendix, Figure S3. The mean probability that a truck would be infected with PRRS virus at the end of the Day 1 when it was used by two farms, and one of the sources of infection was a finishing farm was 0.352. The mean probability marginally increased with an increase in the number of farms that the truck had been shared with on that day. Similarly, the probability of a truck remaining infected did not differ much for truck use across the three different production types. In the case of a 'random' truck (i.e. one for which the number of times it had been used for transportation during the first day was not known), the mean probability was equal across the three production types.

When decay of the virus over time was incorporated in the model, the outputs suggested that the mean probability that a truck would still remain infective after 15 or 30 hours of use during warmer months, from a contamination acquired on Day 1 and without visiting any other infectious farms on subsequent days, was not much different from the probability on Day 1 (Table 5.3). The mean probability decreased by 0.034 and 0.035

(approximately 9%) in the 15 hours of truck use subsequent to Day 1, when the truck had been used by either a nursery or finishing farm respectively, and by 0.049 (13%) when it had been used by a farrowing farm. Similarly, for the next 30 hours after Day 1, the mean probability of infection decreased by 0.06 for nursery and by 0.075 for finishing and farrowing farms in comparison to Day 1. For colder months, the virus can remain viable for around 112 hours, so once contaminated on Day 1 the trucks were expected to remain contaminated for around five additional days.

With respect to the three cleaning protocols evaluated in this study, washing on its own reduced the mean probability of a truck remaining infected by 0.017 (for example, the probability for S.fa= 0.377, decreased to 0.360 with application of washing), while washing with disinfection decreased the mean probability by 0.22 (approximately 60%). However, washing and disinfection followed by overnight drying had by far the highest impact, lowering the mean probability of infection by more than 90%, to around 0.03, irrespective of the production type for which the truck had been used (Figure 5.3). The distributions of probabilities associated with a truck remaining infected after the application of each of the three cleaning and disinfection protocols, for the scenario involving finishing farms, are presented in Figure 5.4. Similar distributions for scenarios without cleaning and disinfection protocols could not be obtained due to the parametrizing of nodes used in those scenarios with step function, which did not allow for the capture of variability in the distribution of these nodes for the scenarios evaluated.

Finally, outputs from the sensitivity analyses suggested that the highest percentage changes were observed for large decrease in farm level or animal level prevalence of

PRRS virus and for a large decrease in the probability of shedding animals in the shipment. However, only a small increase or decrease in the mean probabilities was observed for smaller increase or decrease in each of the parameters evaluated (farm level prevalence, animal-level prevalence, and the probability of animals which were shedding the virus in any particular shipment (Table 5.4 and Figure 5.5). Similarly, large increases (2x and 4x) in the minimum number of infectious animals (N_{ani}) required to contaminate the truck with PRRS virus resulted in only a small decrease in the mean probability of infection.

The MCMC error was less than 5% of the posterior standard deviation for all of the reported scenarios and nodes, which suggested that the model had been run for a sufficient number of iterations, and 20,000 iterations with a burn-in period of 1,000 for each chain was sufficient to allow the models to converge with sufficient sample size for posterior inference. The convergence of the model assessed with the history plots (Appendix, Figure S3) suggested that chains stabilized. Additionally, the scale-reduction factor was less than 1.05 for all the nodes and scenarios evaluated, suggesting that the model converged. The shrinkage plots (Appendix Figure S4), showing the evolution of the scale reduction factor with an increase in the number of iterations, also suggest that the MCMC models had converged after around an initial 4,000 iterations, following the burn-in period of 1,000 iterations, for most of the nodes. Furthermore, the autocorrelation plots (Appendix, Figure S5) indicated that the correlation between every draw with its lag decreased with an increase in the number of iterations, which again suggested convergence of the model.

5.5 Discussion

This analysis has attempted to assess the risk for contamination with PRRS virus of shipment trucks used for the transportation of pigs. To do so, a baseline model was first developed to assess the likelihood that trucks used for shipment of pigs will become contaminated and remain infected with PRRS virus at the end of Day 1. The baseline model was extended to explore a number of what-if scenarios, including variations in the number of times a truck was used on a day, the farm and animal level prevalence of PRRS virus, the size of the shipment on a truck, the probability of shedding animals in the shipment, and the period of travel involved. Additionally, the model was extended to quantify the probability that the truck would remain infected on subsequent days, once it became contaminated, but without visiting any other infected farms, by including decay of the virus over time in the model. We also attempted to evaluate the efficacy of commonly used cleaning and disinfection protocols in eliminating this virus from PRRS virus contaminated trucks.

Based on this model, the estimated probability of a truck being infected at the end of a day slightly increased with an increase in the number of visits the truck made on a given day, however, there were not major differences in the probabilities for scenarios when the truck was used by either farrowing, nursery or finishing farms. The likely explanation for the increased risk with an increase in the number of visits of a truck is that the probability that the truck will visit at least one infected farm increases with the number of visits. The two parameters that were different in the model among the three production types were shedding percentage and shipment size. The sensitivity analysis suggested that the model was less influenced by changes in shedding percentage, unless

it was a very large change, and that above a certain threshold for this parameter, the model behaved similarly. This fact explains why very limited differences in risk were observed among the three production types. Similarly, while separate shipment size distributions were specified for the three production types, in most cases the shipment size was very large and typically reached the minimum number of animals required to characterize the trucks as being contaminated; as such this parameter also had little impact in terms of overall differential risk among the three production types.

The model suggested that only a very small proportion of trucks would eliminate the virus by simply washing the vehicle, while washing followed by disinfection should clean the virus from just over half of the trucks. Washing and disinfection, followed by overnight drying, had the highest impact; resulting in the removal of PRRS virus from a large majority of contaminated trucks. One possible explanation for the high efficacy of this protocol may be as follows. Washing alone can reduce the amount of debris and organic matter but cannot eliminate the virus, while washing followed by disinfection can be useful when the surfaces are free from organic matter. However, the addition to drying can eliminate the virus from contaminated surfaces by eliminating the residual virus that persists after washing and disinfection has occurred (Dee et al., 2005b). Findings from our study slightly contrast with those observed in the experimental studies (Dee et al., 2004a; Dee et al., 2004b), from which we took the data for our study. In the experimental study, washing had no effect at all, washing and disinfection was effective in around a quarter of replications, while washing, disinfection and drying resulted in the elimination of the virus in all replications. This small difference observed

in current study than from previous experimental study was due to the introduction of uncertainty and stochasticity into the model.

Finally, the model suggested that, during warmer months, a slight decrease may occur in the probability that the trucks will be contaminated on the following day as some trucks may get rid of the virus on the following day simply due to the decay of the virus. However, most of the contaminated trucks on Day 1 will be infective for at least the next 30 hours. Again this finding was associated with shipment size. And as our characterization of trucks to be infective for the next 15 or 30 hours was based on double or quadruple number of shedding and infectious animals on the trucks respectively which we used as a proxy for infectious dose of the virus, most of the trucks, due to large shipment sizes, qualified to have four or eight infectious and shedding animals on them. In colder months, when the virus can survive much longer (Linhares et al., 2012), a truck will tend to remain infective for around five days once it has become contaminated. Cleaning and disinfection of trucks to eliminate PRRS virus is thus, rightly, considered crucial during winter months (Dee et al., 2002a; Dee et al., 2005a) when the virus exhibits increased survival. However, our study suggests that it should not be ignored during the warmer months as the likelihood that trucks will remain infected for a number of days following shipment from an infected farm is substantial.

We were unable to quantify the viral load on trucks due to the fact that data on the amount of PRRS virus that is typically shed was not available. Instead we classified trucks in terms of whether they were likely to have sufficient viral load to be able to transmit the infection, based on work by Dee and colleagues (Dee et al., 2004b), using

shipment size as a proxy for viral load. Shipment size was linked to PRRS viral load on the trucks in terms of a dose-response relationship which further affected the time that the truck would likely remain infected with the virus. Even with the decay of the virus over time, trucks that carried larger shipments from infected farms can remain infectious for a number of subsequent days and have sufficient viral loads to infect susceptible animals.

The sensitivity analysis attempted to identify the most influential parameters on the probability of truck infection; particularly around those parameters whose values were estimated based on experts' input. However, the outputs suggested that for small incremental changes for the farm level prevalence of PRRS virus, for the animal level prevalence of the virus and the percentage of shedding animals in the shipment, the model outcome (mean probability for truck infection) was not greatly affected. The sensitivity analysis, when taken in the sense of comparing a number of what-if scenarios that could lead to massive drop in the probability that a truck can remain infected at the end of Day 1, indicated that either decreasing the farm level prevalence of the virus to 10% or decreasing the animal level prevalence of the virus to the same level could decrease the probability for truck infection by more than half. These two findings may have practical significance towards controlling the spread of PRRS virus via shared transport.

Despite making several simplifying assumptions, we believe the model has captured the underlying pathways leading to the contamination with PRRS virus of the trucks used in the transportation of pigs on Canadian farms and from which infection can be transmitted to susceptible pigs. However, we have only presented point estimates for the

probability of truck infection and could not produce a distribution around that estimate, due to use of the step function in the model, which resulted in a binary model outcome. Due to the lack of available data, the current model did not include pathways leading to the eventual transfer of infection from such trucks to susceptible pigs or naïve farms. However, the model could be further extended to elucidate such probabilities, as well as to estimate the indirect contact transmission probability of spreading the PRRS virus via the sharing of trucks. A similar approach could be utilized in understanding the risk of truck sharing on the spread of other swine diseases where transportation has been implicated as a medium for viral spread, as appears to be the case for porcine epidemic diarrhoea (Lowe, 2014).

Findings from this study have value to the swine industry in Canada as they should help producers to make informed decision regarding the sharing of trucks among farms, as well as in guiding the selection of cleaning protocol for trucks. Given the current truck sharing patterns among swine farms in Canada, where for more than half of the shipments on any given day, the same truck has been used on more than one farm (Thakur et al., 2014), together with current biosecurity practices around truck cleaning in Canada, where only around one third of the trucks used for the shipment of pigs are cleaned after every shipment (Lambert et al., 2012b), the current model suggests that there is a substantial risk for spread of PRRS virus through contaminated trucks. This risk could be largely eliminated either by properly washing, disinfecting and drying trucks between successive shipments, by significantly decreasing the farm or animal level prevalence of the PRRS virus, or by using designated trucks for each farm in an attempt to minimise sharing among farms.

5.6 References

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Table 5.1 List of nodes/ parameters, process models, prior distributions and observed data with source and references used to estimate the probability that a truck will be infected with PRRS virus at the end of a working day.

Nodes/ Parameters	Notation	Definition	Process Model	Priors	values/ distribution	Reference
Truck use	Tr.use	The probability that the truck is used between two, three or four or more farms in a single day	**Fixed**		Two=0.5 Three=0.18 ≥Four =0.32	Pilot Pig Traceability Data (Thakur et al., 2014)
Farm Positives	F.Pos.2	The number of farms infected with PRRS virus out of the two farms visited by the truck	Binomial	Beta(1,1)		Assumption of 50% farm level prevalence (F.Prev) of PRRS virus
	F.Pos.3	The number of farms infected with PRRS virus out of the three farms visited by the truck	Binomial	Beta(1,1)		
	F.Pos.4	The number of farms infected with PRRS virus out of the four farms visited by the truck	Binomial	Beta(1,1)		
Farm Infection	F.inf.2 /3 /4	The probability that at least one of the farm was infected when the truck was used by two / three / four farms				
	Comb.Prob	The probability that at least one of the farms the truck visited was infected, when the number of farms it visited was unknown	F.inf.2*0.49 +F.inf.3*.19 +F.inf.4*.32			
Animal level prevalence	$A.Prev._k$	The prevalence of PRRS in the batch of animals shipped	Fixed		0.8	Experts' judgement

Table 5.1 (continued)

Nodes/ Parameters	Notation	Definition	Process Model	Priors	values/ distribution	Reference
Shedding animals	$Shed.ani._k$	The probability of shedding animals in a batch of animals shipped	Fixed		0.2, 0.5,0.8	for farrowing, nursery and finishing farms based on Expert's judgement
Shedding prevalence	$Shed.prev._k$	The probability of infectious and shedding animals in a batch of animals shipped	Prev * Shed.ani			
Number of shedding animals	N_{anik}	Number of infectious and shedding animals on a truck to characterize it as contaminated	2	Fixed		Dee et al's study
Minimum number of animals	Min_{anik}	The minimum number of animals required on a truck to have at least 2 infectious and shedding animals in a batch of animals shipped (based on shedding proportion)	Hypergeo metric			
	N_{ani1k}	Number of infectious and shedding animals on a truck when the number of animals on the truck is equal to Min_{ani}	Hypergeo metric			
	$N_{ani1.stepk}$	The probability that a truck with Min_{ani} has at least 2 infectious and shedding animals				

Table 5.1 (continued)

Nodes/ Parameters	Notation	Definition	Process Model	Priors	values/ distribution	Reference
Shipment size	$Ship_{sizek}$	The distribution of shipment size for shipments from the three production type	Uniform	(1,622) (1,700) (1,256)		for farrowing, nursery and finishing farms respectively Pilot Pig Traceability Data
Minimum Shipment Size	Min_{ship}.Fa/Nu/Fi	The probability that the truck has more animals than Min_{ani} if it was coming from a farrowing / nursery / finishing farm				
Travel time	Travel.time	The distribution of travel time for trucks, which was obtained by assuming a normal distribution for travel time with min, mode and max values of 0.5,2,6 respectively	Normal	Normal (2.43,1.22)		Experts' judgement
	Travel	The probability that the travel time was more than two hours in order to qualify the truck to be infective				
Infective Dose	Inf.dose	The probability that the truck has an infective dose of virus, which depends on shipment size and travel time	Travel* Min_{ship}			

Table 5.1 (continued)

Nodes/ Parameters	Notation	Definition	Process Model	Priors	values/ distribution	Reference
Truck Infection	Tr.inf	The probability that the truck is infected at the end of the day's work	Tr.use*F.inf*Inf.dose			
Truck wash efficacy	W.efficacy	The probability that washing clears the virus from the truck	Binomial	Beta (1,1)	N.Prot=0 N.Wd=10	
Truck wash and disinfection efficacy	Wd.efficacy	The probability that washing and disinfection clears the virus from the truck	Binomial	Beta (1,1)	N.Prot=6 N.Wd=20	
Truck wash, disinfection and dry efficacy	Wdd.efficacy	The probability that washing, disinfection and drying clears the virus from the truck	Binomial	Beta (1,1)	N.Prot=10 N.Wdd=10	
Truck Infection after wdd	Tr.inf.wdd	The probability that the truck is still infected after washing, washing and disinfection and washing, disinfection and drying	Tr.inf*W.efficacy			

N.Prot= Number of clean trucks after wash, wash and disinfection or after wash, disinfection and dry, N.W=total number of trucks washed, N.Wd=total number of trucks washed and disinfected, N.Wdd=total number of trucks washed, disinfected and dried

Table 5.2 Scenarios created to evaluate the probability that a truck will be infected with PRRS virus at the end of a working day.

Name of the scenarios	Truck used between farms	Truck: Washed/ disinfected/Dried	Truck used by
S.2.fa	2	No	Farrowing
S.2.nu			Nursery
S.2.fi			Finishing
S.3.fa	3		Farrowing
S.3.nu			Nursery
S.3.fi			Finishing
S.4.fa	4 or more		Farrowing
S.4.nu			Nursery
S.4.fi			Finishing
S.fa	Combined		Farrowing
S.nu			Nursery
S.fi			Finishing
S. fa.w		Wash only	Farrowing
S.nu.w			Nursery
S.fi.w			Finishing
S.fa.wd		Wash and Disinfect	Farrowing
S.nu.wd			Nursery
S.fi.wd			Finishing
S.fa.wdd		Wash, Disinfect and Dry	Farrowing
S.nu.wdd			Nursery
S.fi.wdd			Finishing

S=Scenario, 2=truck used by two farms, 3=truck used by three farms, 4=truck used by four or more farms, combined=trucks used by either 2, 3, 4 or more farms, w=trucks washed, wd=trucks washed and disinfected, wdd=trucks washed, disinfected and dried, fa=truck used by farrowing farms, nu=truck used by nursery farms and fi=trucks used by finishing farms

Table 5.3 Probability that a truck will remain contaminated with PRRS virus in subsequent time periods during warmer months.

Nodes/ Scenarios	Mean probability on Day 1	Mean probability for next 15 hours after Day 1	% decrease in mean probability from Day 1	Mean probability for next 30 hours after Day 1	% decrease in mean probability from Day 1
S.fa	0.377	0.328	13.0	0.303	19.6
S.nu	0.389	0.355	8.7	0.328	15.7
S.fi	0.393	0.358	8.9	0.320	18.6

Table 5.4 Sensitivity analysis for the probability that a truck will be infected with PRRS virus at the end of a working day.

Scenarios	Notations	Parameter				±% change in input parameter	Mean probability	±% change in mean probability
		N_{ani}	F. Prev	A.Prev	Shed.ani			
S.4.fi	1344	2	50	80	70	NA	0.444	Baseline scenario
Change in N_{ani} to 4	2344	4	50	80	70	100%	0.398	-10.4
Change in N_{ani} to 8	3344	8	50	80	70	200%	0.365	-17.8
Change in farm level prevalence to 10%	1144	2	10	80	70	-80	0.162	-63.5
Change in farm level prevalence to 30%	1244	2	30	80	70	-40	0.359	-19.1
Change in farm level prevalence to 70%	1444	2	70	80	70	40	0.469	5.6
Change in animal level prevalence to 10%	1314	2	50	10	70	-87.5	0.160	-64.0
Change in animal level prevalence to 30%	1324	2	50	30	70	-62.5	0.390	-12.2
Change in animal level prevalence to 50%	1334	2	50	50	70	-37.5	0.428	-3.6
Change in animal level prevalence to 100%	1354	2	50	100	70	25	0.464	4.5
Change in shedding animal (Shed.ani) to 10%	1341	2	50	80	10	-85.7	0.181	-59.2
Change in shedding animal (Shed.ani) to 30%	1342	2	50	80	30	-57	0.400	-9.9
Change in shedding animal (Shed.ani) to 50%	1343	2	50	80	50	-28.6	0. 430	-3.15
Change in shedding animal (Shed.ani) to 90%	1345	2	50	80	90	28.6	0.470	5.8

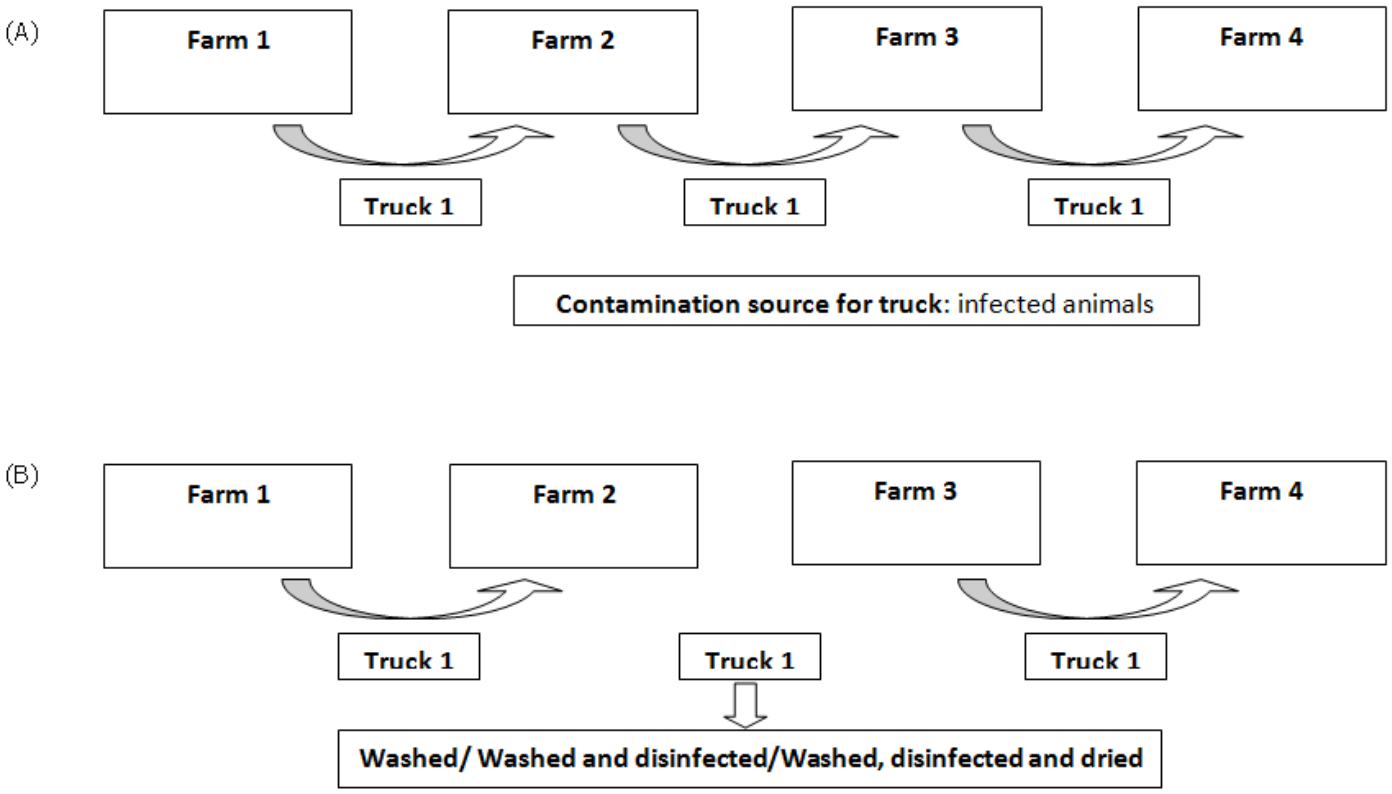

Figure 5.1 Pathways of truck sharing between farms, [A] without cleaning and disinfection, and [B] with cleaning and disinfection, within a one day time period. One truck may be used between two farms or more than two farms within the time period considered in this risk analysis exercise.

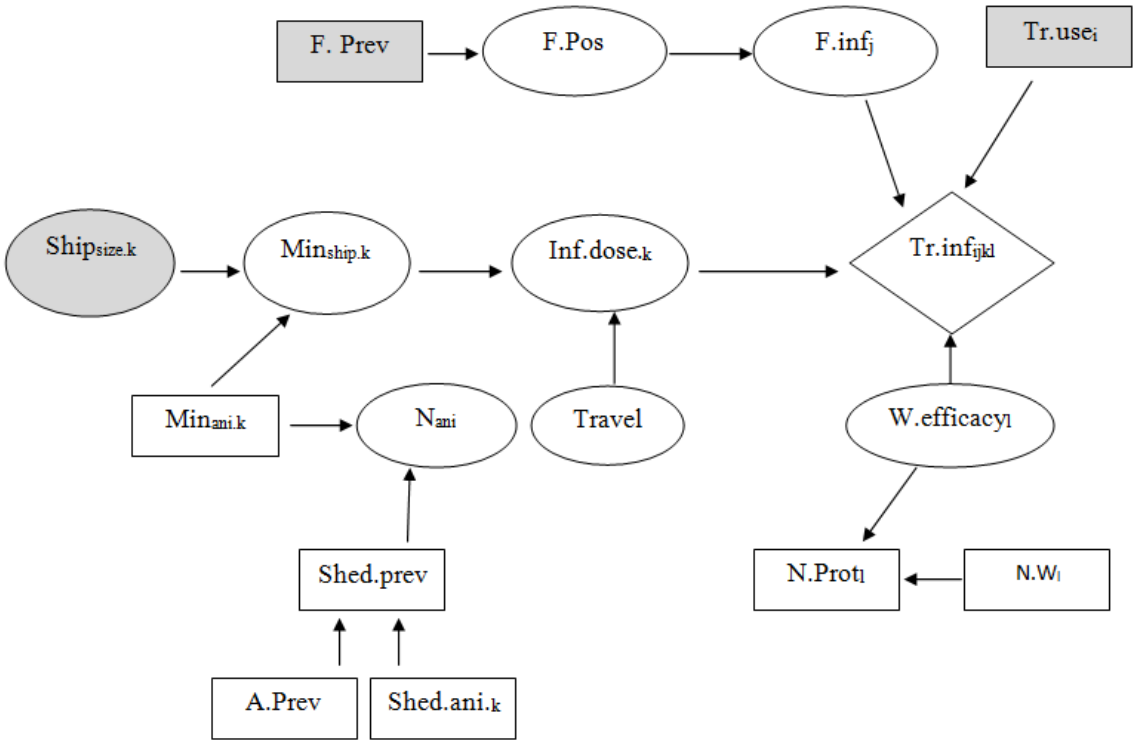

Figure 5.2 Schematic representation of the Bayesian Network to estimate the likelihood of contamination of shipment trucks with PRRS virus and to evaluate the efficacy of various cleaning and disinfecting protocols for removal of PRRS virus from contaminated trucks.

Fixed nodes are shown in rectangles while stochastic nodes in ellipsoids. The diamond-shaped node represent outcomes that are estimated by the model. Nodes with gray shading represent prior information. The model represents a truck$_i$, that can have visits$_j$ (2,3, or 4 or more) on a day and can ship animals from production types$_k$ (farrowing, nursery or finishing) of swine farms and can be cleaned by using protocols (wash, wash and disinfect, or wash, disinfect and dry).

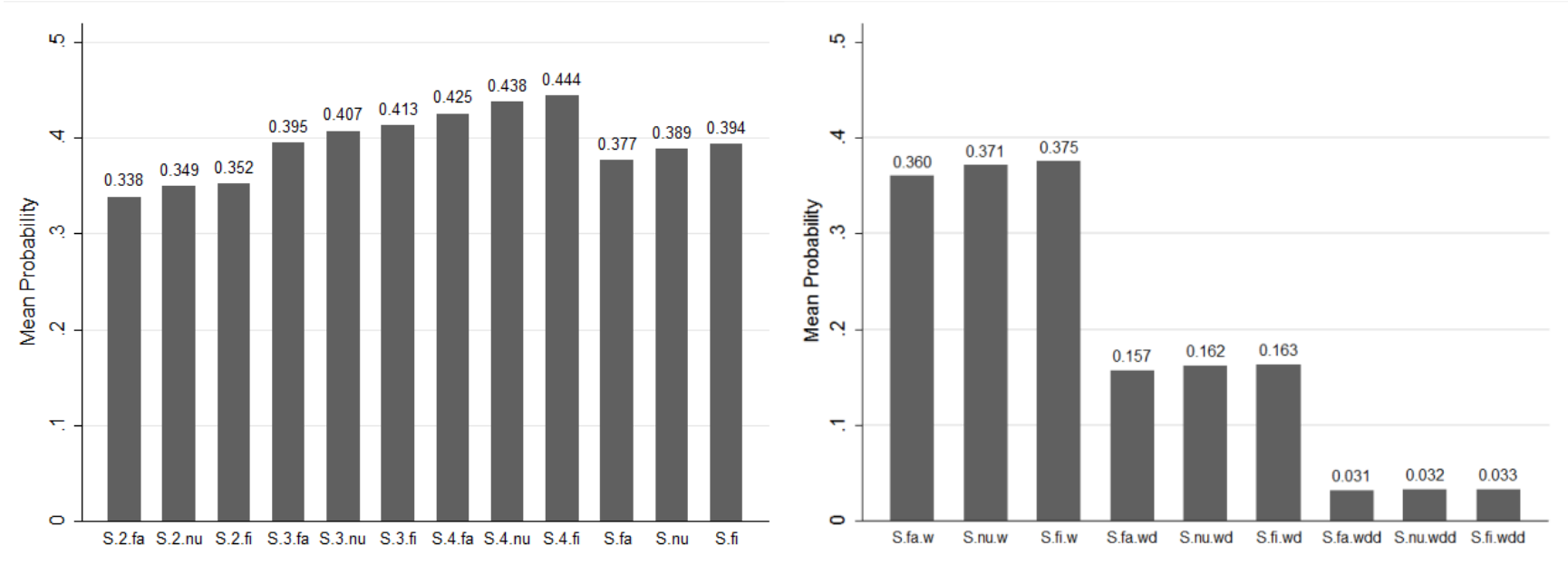

Figure 5.3 Mean probabilities for contamination of trucks with PRRS virus at the end of Day 1, for several scenarios depending on the number of times the trucks were shared and the production type of the PRRS virus infected farm, (A) without cleaning and disinfection of trucks and (B) with application of one of the three cleaning protocols evaluated in the study.

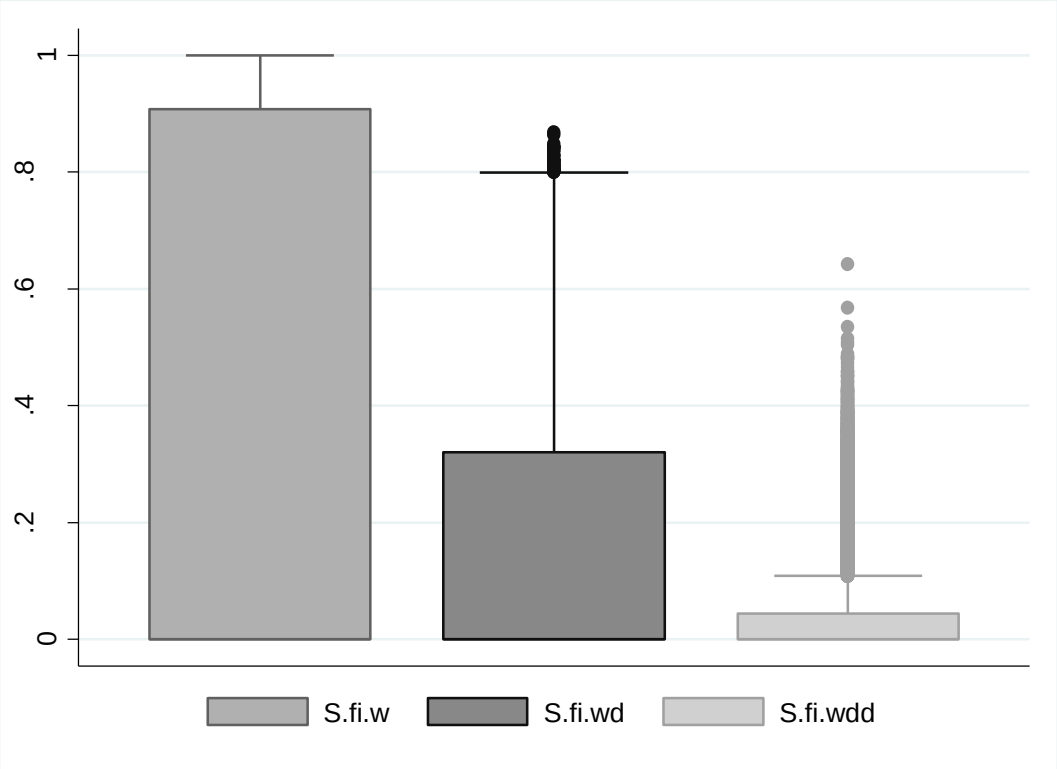

Figure 5.4 Distribution of posterior probabilities for contamination of trucks with PRRS virus after application of one of the three different cleaning and disinfection protocols (w: washing, wd: washing and disinfection and wdd: washing, disinfection and drying) for a truck that was used by an infected finishing (fi) farm, where the boxes represent inter quartile range of the distribution.

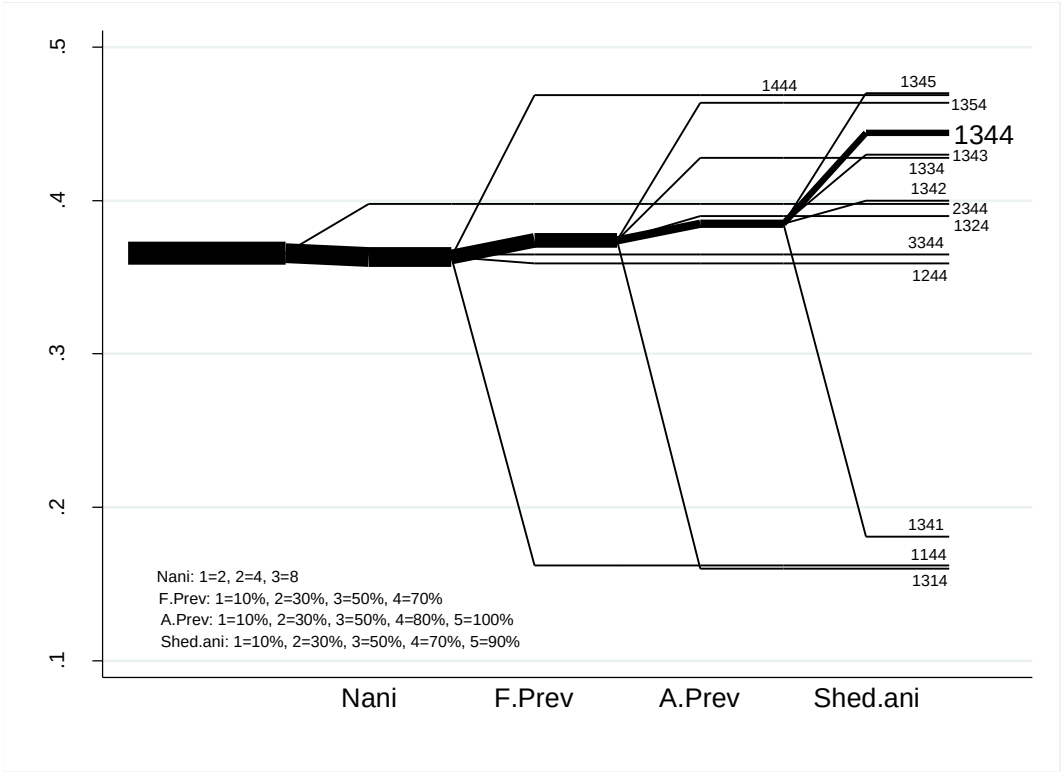

Figure 5.5 Risk plot showing sensitivity of the mean probability that a truck will be infected with PRRS virus to changes in key model parameter values to that of the baseline model (1344): Nani (minimum number of infectious and shedding animals required on the truck), farm level prevalence (F.prev), animal level prevalence (A.Prev) of the virus and the probability of shedding animals (Shed.ani) on the truck respectively.

Chapter 6 General Discussion, Limitations and Future Directions

The main focus of the research reported in this thesis was to simulate the spread of PRRS virus in order to better understand the transmission dynamics of the virus as a result of the movement of pigs between Canadian swine herds. A key goal was to elucidate the relative impact of direct and indirect contacts on the spread of PRRS virus, or indeed other contagious diseases of swine with similar epidemiological characteristics to those of the PRRS virus. To accomplish this network analysis (NA) tools were used to determine direct (via the movement of pigs) and indirect (via the sharing of shipment trucks) contact patterns between Canadian swine farms, based on historical information that had been collected as part of a pilot traceability project in the swine industry of four Canadian regions. The contact rates obtained from the network analysis study were used to simulate a farm level model for the spread of PRRS virus via the movement of animals and sharing of trucks between farms. Thereafter, the extent and patterns involved in the spread of PRRS virus via direct (movement of animals) and indirect contacts (sharing of trucks) among swine farms in Ontario, Canada were explored using a variety of simulation models. The first simulation study utilized a spatially-explicit model (NAADSM) that did not consider the contact network structure among farms. However, previous studies had suggested that the contact network structure among farms can have significant impacts on the way in which disease will spread (Keeling, 2005; Keeling and Eames, 2005b; Dangerfield et al., 2009). To this end, the network structure identified for swine movement in four regions of Canada was studied, which corresponded to small-world and scale free topologies, similar to other studies within Canada and from other geographical regions (Nöremark et al., 2011b; Rautureau et al., 2012a; Büttner et al., 2013b; Dorjee et al., 2013). Based on the identified network

structure of swine farms the second simulation study was conducted, so that the impact of network structures within the swine industry on the pattern and extent of PRRS virus spread in a population of hypothetical Canadian swine farms could be evaluated. The two main simulation studies described in this thesis both highlighted the impact of indirect contact, via the sharing of trucks among farms, on between-farm transmission of PRRS virus. The final chapter assessed the likelihood that a given truck used for the transportation of pigs would be contaminated with PRRS virus and also evaluated the likelihood that these trucks would remain contaminated over the succeeding few days in the absence of any new source of PRRS virus contamination. The key findings from these studies, and their implications, are discussed in this chapter together with an outline of some limitations associated with these studies and considerations for future research.

6.1 General Discussion

The connections between swine farms, at least those explored in this study, appeared to align well with the hierarchical organization of the swine industry, in which pigs at different stages of growth move unidirectionally from one stage of production to the next. Additionally, the NA study explored the indirect contact structures that exist as a result of the sharing of trucks among farms, and suggested that a large number of trucks were being shared between farms for the shipment of pigs. Indeed, for more than half of the shipments on any given day, the same truck was used for more than one shipment, indicating that many farms that are not directly connected via the movement of animals are connected by this indirect path (which ultimately decreased the average number of

links required to reach any pair of farms in the network). This level of truck sharing between farms should be a concern for the swine industry in terms of the spread of a number of infectious agents, such as PRRS virus and Porcine Epidemic Diarrhea (PED), particularly if trucks are not adequately cleaned and disinfected between successive shipments. Furthermore, the NA study provided contact parameters for the swine industry in Canada, which were used in the simulations of virus spread, and these parameters may be helpful in parametrizing future simulations studies that model the likely spread of other infectious diseases within the Canadian swine industry. The simulations of PRRS virus spread in this thesis used maximum out-degree, the number of unique contacts a farm has, to estimate the mean contact rate between farms. Simulations involving contact rates derived from maximum out-degree are likely to provide more reliable estimates of epidemic size than would be the case when contact rates are based on shipment frequency (Dubé et al., 2008). The argument for using out-degree, over shipment frequency, is that shipment frequency does not exclude multiple shipments going to the same farm and will therefore tend to *over-estimate* the contact rate between farms; ultimately resulting in larger sizes of modelled epidemics. In contrast, simply using out-degree will likely underestimate epidemic size (Dubé et al., 2008). Therefore, maximum out-degree for each production type was used in the estimation of contact rates, on the basis that this will tend to provide a better estimate of contact rate than either shipment frequency or simple farm-level out-degree.

Based on the contact rates obtained from the NA study, the spread of PRRS virus (via direct and indirect contact), was simulated and described in Chapters 3 and 4. In this thesis, two modeling approaches were considered for between-farm spread of PRRS

virus, namely, spatially-explicit modelling (NAADSM) and network-based modelling (in AnyLogic).

The NAADSM model evaluated several hypothetical scenarios for between-farm spread of PRRS virus that considered direct and indirect contact between farms, together with the production type of the farm in which the infection was seeded. This model highlighted the relative importance of direct and indirect contact, as a result of the sharing of trucks that were assumed not to be cleaned between successive shipments, on between-farm transmission of PRRS virus.

The use of a network-based model highlighted the importance of understanding and incorporating realistic network structures among the individuals of a population when developing infectious disease spread models. The findings suggested that any outbreak in a scale-free network will spread rapidly and will result in the largest epidemic size, due to the presence of "hubs" (Dube et al., 2011) in the scale-free network. This result is consistent with findings from other similar studies (Rahmandad and Sterman, 2008; Rahmandad et al., 2011). The spread of the virus in small-world networks resulted in lower epidemic sizes, as farms in this type of network tend to form small groups and have limited contact with members of distant groups in the network. In this study, the epidemic size observed for spread of the virus in random networks was similar to those observed for small-world networks, which contrasted with reports from other studies where outbreaks on random networks resulted in similar epidemic sizes to those seen in scale-free networks (Keeling and Eames, 2005a; Shirley and Rushton, 2005b; Rahmandad and Sterman, 2008; Rahmandad et al., 2011). Random networks are characterized as having equal probability of connection among individuals in the

network (Erdős and Rényi, 1960). The key difference in the construction of random networks in this study, compared to other reported studies, was that the average number of connections between farms was much lower. When the average number of connections was increased, as part of the sensitivity analysis, this did indeed lead to much larger epidemic sizes.

Both types of models discussed in this thesis simulated disease spread at farm level and used similar parameters. However, there are some fundamental differences between the two approaches. For the network-based model, the direct contact between farms was limited to only those farms that were connected as per the construction rules of the network structure specified. On the other hand, for the NAADSM model, no network structure was imposed, so farms were allowed to contact any other farm randomly, provided they were in the same contact group (for example, any farrowing farm was allowed to contact any other nursery farm). Additionally, for the NAADSM model in this thesis, the distance distribution over which farms can have contact had negligible impact on the disease progression which suggested location of farms may have very little influence on long range geographic spread of PRRS virus. This was one of the key reasons for the quantitatively different outputs from these models; specifically, the impact of indirect contact was higher in the case of the network-based model than was the case for the NAADSM model. Strictly, it may not be reasonable to directly compare outputs from models that were simulated based on different underlying principles; however, it can add value for the practical purpose for selecting between modeling platforms. It should be noted that although the outputs from these two modeling platforms were quantitatively different, the pattern of outbreaks remained similar across

the AnyLogic and NAADSM models. Outbreaks initiated within farrowing farms were most likely to have the highest impact on the overall epidemic size and the incorporation of indirect contact significantly increased the epidemic size in all models explored. Thus, the importance of comparatively simpler models such as NAADSM cannot be discounted, especially when the objective of the exercise is not to attempt to make a quantitative prediction but, rather, to understand the relative importance of direct and indirect contacts on the extent and progression of outbreaks. NAADSM is also simpler to set up and may be better suited for use by those with limited computer programming skills or in cases where detailed contract structure data are not available.

The major focus of this thesis was to elucidate the transmission dynamics of PRRS virus due to the movement of pigs between Canadian swine herds. Hence, the scope of the simulation studies in Chapters 3 and 4 were limited to an evaluation of the relative impact of direct and indirect contacts between farms on the spread of PRRS virus. The incorporation of indirect contact, for both NAADSM and network-based models, resulted in much larger epidemic sizes than those produced by direct contact or indirect contact separately, suggesting that the incorporation of both contact types has a synergistic effect on disease spread. At the most fundamental level, the sharing of trucks could lead to connections between farms that were never directly linked via animal movement or that did not typically receive animals. With the incorporation of indirect contact, the virus could spread in a multidirectional fashion linking farms among the various production types. Thus, the protection provided by a farm's position within the hierarchical structure was no longer maintained. However, the impact of indirect contact

was less pronounced in the NAADSM models compared to models in which network structure was incorporated.

Two other studies using different methodological approaches have also identified the role of shared trucks in the spread of PRRS virus among Ontario swine herds (Kwong et al., 2013; Arruda et al., 2015). These studies reinforce the findings of this thesis and highlight the importance of indirect contacts as a route for transmission of PRRS virus. Kwong et al (Kwong et al., 2013) identified that the use of the same trucks was one of the three most important factors in the spread of one particular genotype of PRRS virus within swine herds in Ontario, while Arruda et al (Arruda et al., 2015) reported that if a farm was a part of a truck network in which at least one other farm was infected with PRRS virus, the odds for being infected with the virus increased. Indeed, this study suggested that 45.6% of farm infections within a network of farms which used same trucks from the same transportation company for the shipment of pigs could be attributed to this mode of transmission. The swine industry in Ontario should take note of these findings and consider implementing interventions such as the use of designated trucks for infected and naive farms, plan more regular visits to assess the health status of farms, and ensure the regular cleaning and disinfection of trucks between shipments, in an attempt to limit the spread of PRRS virus via this indirect route.

The first three research chapters of this thesis suggested that a high degree of truck sharing between farms in the shipment of pigs could have a significant impact on the between-farm spread of PRRS virus, however, some gaps in knowledge regarding the associated risks, motivated further study using the Bayesian Analysis of Chapter 5. The main focus of this study was on estimating the probability that a truck, used for the

shipment of pigs, would be contaminated with PRRS virus at the end of any given day. This work suggested that it was very likely that most of the trucks used by swine farms for the shipment of pigs would become contaminated with the PRRS virus, given the current disease infection status of PRRS virus and the truck sharing patterns typically seen in Canadian farms. Additionally, this study suggested that most of the trucks that become contaminated will remain infected for around a week, during colder months, if no cleaning or disinfection is applied. In warmer months due to viral decay, some of the trucks may get rid of the virus reasonably quickly; however, most of the trucks will likely remain infected for at least two more days from the time of initial contamination. This study further suggested that to decrease the probability for truck infection by more than half, either the farm-level or the animal-level prevalence of the virus needed to be lowered to around 10%. The study also evaluated the impact of three commonly used cleaning and disinfection protocols in eliminating the virus from contaminated trucks. The findings suggested that washing and disinfection followed by overnight drying was a much more effective approach than only washing, or washing with disinfection. The use of a Bayesian network in this study allowed for the combination of different sources of information and the propagation of uncertainty in the model (Czado and Brechmann, 2014), as well as a relaxation of the assumption, adopted in most risk analysis models, of conditional dependence between nodes (Albert et al., 2008).

6.2 Limitations

The ability of a model to represent reality depends on the accuracy and completeness of the model and the parameters used. However, gaps in knowledge on several

epidemiological determinants governing disease processes present difficulties in producing truly predictive models (Taylor and Gate, 2003). The development of models, in collaboration with subject-matter experts, is instrumental in capturing some of the undocumented parameters and improving the reliability of the model (Taylor and Gate, 2003). An infectious disease model is considered internally valid if the outcomes of the model are epidemiologically plausible for the study population considered and make biological sense under the parameters used to simulate the model (Dubé et al., 2007). The outcomes of the models for between-farm PRRS virus spread described in this thesis are epidemiologically justifiable. Even though the models presented in this thesis utilized empirical contact structures, the studies involved to extract the contact structure utilized limited data and were not very recent. Similarly, some of the other parameters were based on experts' suggestions. Additionally, the outputs from the simulated models could not be validated in the absence of outbreak data that could be linked with the movement of pigs. However, even in the absence of data to validate the model, disease spread models may still be a useful tool for epidemiologists and decision makers by providing insights into the mechanisms of disease spread (Taylor and Gate, 2003). Several published models have been useful in understanding the disease spread process as well as in evaluating 'what if' scenarios for several pathogens, such as highly pathogenic avian influenza virus (Patyk et al., 2013), H_1N_1 influenza virus (Dorjee et al., 2014) and FMD virus (Dubé et al., 2007; Sanson et al., 2014).

For the NAADSM model, it should be noted that the version of the software used for this thesis, did not allow for the selection of different farms in which the infection could be seeded. However, this limitation becomes irrelevant unless local or aerosol

transmission is being considered, and these two transmission modes were considered to be beyond the scope of the current research. While aerosol transmission was not considered, the impact that this mode of transmission has on between-farm spread of PRRS virus would likely be limited, as studies have suggested that it can influence local, rather than long distance, spread of the virus (Le Potier et al., 1997; Goldberg et al., 2000; Mondaca-Fernández et al., 2006; Lambert et al., 2012a). For network-based models, one limitation worth noting was that the software used to simulate disease spread did not allow for the small-world networks to reflect the precise characteristics of the observed network connections among swine farms. For these reasons making any quantitative inferences based on the outcomes of these models may require some caution. Instead, the findings from these studies should be considered as a qualitative guide to understanding the pattern and magnitude of likely PRRS virus outbreaks under the scenarios explored. Similarly, for the Bayesian risk model, several parameters (farm level prevalence, animal level prevalence and shedding animals) were based on assumptions. However, sensitivity analysis across a range of values for these parameters suggested that the model outcome was not particularly sensitive to changes in the values of these parameters. It should also be noted that viral load on shipment trucks could not be quantified, due to insufficiency of data, and that the number of infectious and shedding animals on the truck was used as a proxy for having sufficient viral load to characterize the truck as being contaminated. One other limitation of the Bayesian model worth noting was the loss of variability in the estimated parameters, for which only point estimates were reported. This was linked to the use of step functions in the

model for several nodes, resulting in binary outcomes rather than in a distribution of estimates for such nodes.

6.3 Concluding Remarks

The studies described in this thesis have provided insights into the pattern of contacts between swine farms and the impact these contacts can have on PRRS virus spread. In addition, the importance of including data on the sharing of trucks among farms in the simulation models has been highlighted, as trucks will tend to connect farms which would otherwise share no connection. In many intensive swine production regions in North America (such as in Minnesota or Ontario), ARC&E programs have been designed to eliminate PRRS virus infection from a particular region or geographical area (Corzo et al., 2010; Arruda et al., 2014). Any such program may benefit from the findings in this dissertation by helping regional disease control managers to better understand the patterns of direct and indirect contacts that swine farms may have, the levels of indirect contact as a result of truck sharing, and the potential impact these forms of contact can have on the spread of the virus in that region. Additionally, findings from this study regarding the high potential for shipment trucks to remain contaminated with PRRS virus for a number of days after they become infected has highlighted the importance of biosecurity measures in preventing the further spread of the virus from infectious farms via shared trucks.

The swine industry in North America has been alarmed by recent outbreaks of PED across a wide geographical region (Stevenson et al., 2013a; Kehrli et al., 2014), with contaminated feed widely considered to be the source of the initial outbreak of the virus

(Pasick et al., 2014). Transportation trucks have been implicated, by the experts in the industry and in a number of initial published reports, in the subsequent spread of the virus across several states and provinces from the initially infected farms (Lowe, 2014). Findings from this study are in line with the opinion of swine experts that, given the high number of farms sharing trucks for the shipment of pigs, it is likely that transportation was the cause of the long distance spread of the PED virus outbreak in such a short time span. This opinion is reinforced by the fact that approximately only one third of such trucks are cleaned and disinfected between successive shipments (Lambert et al., 2012b). Future studies to evaluate the impact of such indirect contact between farms on the spread of the PED virus may benefit from the methods and approaches discussed in this dissertation.

6.4 Future Directions

Since animal movement networks are dynamic in nature, it is valuable to analyze movement data over a reasonable period of time to investigate any structural changes that might take place in the network. Thus, future research which had an objective to capture movement data linked to swine on a continuous basis, and that could be used to update the characteristics of swine movement networks in Canada, would be of great benefit to industry and policy makers. Any such study could indicate recent structural changes in the networks typical of swine movement and elucidate current pattern of truck sharing among swine farms, which may or may not be different from that which has been described in this thesis. Incorporation of local spread, aerosol spread and other forms of indirect contacts within a PRRS virus spread model were beyond the scope of

this dissertation. However, the inclusion of other potential modes of transmission of the virus within a model would provide a more detailed understanding of likely between-farm transmission of the virus and would be helpful in evaluating the relative impact of each of these modes of transmission. Similarly, breeding farms were not included in the models described in this thesis, future studies can assess the risk of disease spread to other farms from breeding farms.

In the current network-based models, trucks could not explicitly represented as agents, rather truck sharing between farms was represented as indirect contact between farms and implemented as a probabilistic link between the relevant nodes. Network-based models, an extension of the agent-based models, explicitly incorporate network structures between individuals (farms in these models) in the population (Keeling and Eames, 2005a; Lanzas and Chen, 2014). However, in an agent based model it would be possible to provide a mechanism by which trucks could be represented as additional agents within the model. This would allow for comparison between the outputs of two different models and assess the impact of adding an additional layer of complexity to the model. Inclusion of trucks as additional agents in the model would allow for the simulation of a scale-free structure for indirect contact. This would be in line with the outcome of the NA study which suggested that trucks shared between farms followed a power-law distribution and would likely result in a more pronounced effect due to indirect contact. It would also be beneficial to extract the links created between farms on a typical run of the NAADSM model, so that these could be analyzed using network analysis tools, to better understand the network structure being constructed inside the NAADSM model.

The Bayesian model described in this thesis did not include pathways that can lead to the spread of infection from contaminated trucks to naive pigs or farms, so future studies could extend the current model to include such pathways, which would better support the estimation of the indirect contact transmission probability of PRRS virus via the sharing of trucks. It would also be useful to find an alternative to the step function used in the Bayesian Network which would allow for the incorporation of variability into model outcomes. Finally, it should be noted that, simulation models provide insights into understanding complex processes and can inform decision making, but models themselves require sound and reliable data and cannot always be a substitute for field-based epidemiological or experimental studies (Kao, 2002). Hence, research studies focused on regular epidemiological data collection and reporting play a vital role in supplementing findings from simulation studies, and their role in guiding the parametrization of simulation studies should never be discounted. For example, under the currently practiced area regional control and eradication (ARC&E) programs for PRRS virus (Corzo et al., 2010), any documentation concerning the sharing of transport vehicles and movement of pigs between farms, as well as the capture of data on PRRS virus outbreaks on farms, could greatly benefit future modeling studies; not only in validating the models, but also by providing updated parameters for model development.

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Appendix

Table S1Contact matrix with probabilities of swine movements between different production types based on total number of shipments as reported in swine movement data

Source farms	Destination farms				
	Farrow to finish (%)	Farrowing (%)	NurseryA (%)	FinishingA (%)	Total
Farrow-to-finish	-	0	25	75	100
Farrowing	-	2	92	6	100
NurseryA	-	-	8	92	100
FinishingA	-	-	5	95	100

Table S2 Contact matrix of truck sharing between farms of different production types based on total number of trucks shared between more than two farms (from swine movement data)

	Farrow-to-finish (%)	Farrowing (%)	NurseryA (%)	FinishingA (%)	NurseryC (%)	FinishingC (%)
Farrow-to-finish	0	0.06	0.14	0.29	0.14	0.29
Farrowing	0.06	2.6	0.94	0.14	0.94	0.14
NurseryA	0.14	0.94	2.3	3.9	2.3	3.9
FinishingA	0.29	0.14	3.9	12.8	3.9	12.8
NurseryC	0.14	0.94	2.3	3.9	2.3	3.9
FinishingC	0.29	0.14	3.9	12.8	3.9	12.8

This matrix represents the percentage of trucks shared among farms of different production types during the entire duration of study, which is later used to calculate weekly indirect contact rates by dividing with the study duration.

Table S3 Mean Contact rate per week among different production types, calculated based on contact matrix and maximum out-degree (from swine movement data) of each production type

Source farms	Destination farms			
	Farrow to finish	Farrowing	NurseryA	FinishingA
Farrow to finish	0	0	0.06	0.17
Farrowing	0	0.01	0.51	0.03
NurseryA	0	0	0.03	0.31
FinishingA	0	0	0.01	0.21

Table S4 Mean indirect contact rate per week between farms of different production types via sharing of trucks used for shipment

	Farrow-to-finish	Farrowing	NurseryA	FinishingA	NurseryC	FinishingC
Farrow-to-finish	0	0.0007	0.002	0.004	0.002	0.004
Farrowing	0.0007	0.03	0.01	0.002	0.01	0.002
NurseryA	0.002	0.012	0.03	0.05	0.03	0.05
FinishingA	0.004	0.002	0.05	0.16	0.05	0.16
NurseryC*	0.002	0.012	0.03	0.05	0.03	0.05
FinishingC*	0.004	0.002	0.05	0.16	0.05	0.16

* The mean indirect contact rates (Supplementary material, Table S4) for these farms (NurseryC and FinishingC) with farms of other production types were derived using the contact matrix presented in Table S3, where nurseryA and nurseryC farms and finshingA and finishingC farms had similar proportion of truck sharing with rest of the production types. Weekly contact rates were obtained by dividing the proportion of truck share with duration of the study (18 weeks) and then multiplying by maximum number of farms sharing a single truck (which represented the worst case scenario).

Table S5 Descriptive summary of the model-generated number of farms infected with PRRS virus and time required to reach the peak epidemic from simulation based on 1000 iterations of scenarios (Set A additional scenarios)

Scenario No.	Scenario Name	Farms Infected: Median (p95)							Epidemic Size: Median (p95)			Week to peak epidemic (p95)
		Overall	Farrowing	NurseryA	FinishingA	Farrow-to-finish	NurseryC	FinishingC	Overall	NurseryA	FinishingA	
2	DC_NA	418 (483)	0 (0)	41 (64)	377 (419)	0 (0)	0 (0)	0 (0)	490 (681)	45 (74)	444 (538)	41 (52)
3	DC_FiA	410 (477)	0 (0)	44 (62)	366 (415)	0 (0)	0 (0)	0 (0)	513 (668)	47 (71)	466 (601)	44 (52)
4	DC_FF	428 (485)	0 (0)	48 (66)	379 (418)	1 (1)	0 (0)	0 (0)	546 (687)	53 (77)	490 (614)	45 (52)
5	DC_NC	42 (51)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)	41 (50)	42 (51)	0 (0)	0 (0)	46 (52)
6	DC_FiC	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)	1 (1)	0 (0)	0 (0)	NA
8	D&IC_NA	802 (983)	3 (9)	86 (124)	421 (451)	3 (8)	47 (90)	242 (301)	963 (1271)	107 (173)	555 (709)	37 (46)
9	D&IC_FiA	825 (978)	3 (6)	93 (125)	418 (448)	4 (6)	53 (91)	254 (302)	1006 (1270)	114 (171)	576 (711)	39 (47)
10	D&IC_FF	856 (1035)	4 (12)	99 (138)	423 (455)	5 (10)	61 (106)	264 (314)	1054 (1345)	126 (204)	594 (722)	41 (49)
11	D&IC_NC	816 (974)	4 (10)	89 (123)	402 (440)	4 (6)	55 (92)	262 (303)	952 (1207)	109 (168)	515 (649)	42 (50)
12	D&IC_FiC	174 (866)	0 (5)	12 (101)	104 (422)	0 (5)	7 (63)	51 (270)	227 (1025)	17 (122)	145 (573)	45 (52)

DC=Direct Contact, D&IC=Direct and indirect contact, NA=NurseryA, FiA=FinishingA, FF=Farrow-to-finish NC= NurseryC, FiC=FinishingC
For median number of farms infected, farms that had multiple infections were counted only once; while for median epidemic size, farms with multiple outbreaks were counted multiple times. For Farrowing, Farrow-to -finish, NurseryC and FinishingC farms, the median epidemic sizes were similar to their respective median numbers of farms infected.
p95= 95th percentile

Table S6 Summary statistics relating to multiple outbreaks of PRRS virus during the period of simulation based on 1000 iterations of scenarios (Set A additional scenarios)

Scenario No.	Scenario Name	Percentage of farms with the indicated number of outbreaks													
		Farrowing		NurseryA				FinishingA			Farrow-to-finish		NurseryC		FinishingC	
		0	1	0	1	2-3	>4	0	1	2-3	0	1	0	1	0	1
2	DC_NA	100	0	83.5	14.5	2.0	0	23.7	53.4	22.9	100	0	100	0	100	0
3	DC_FiA	100	0	82.3	15.9	1.8	0	25.9	53.6	20.5	100	0	100	0	100	0
4	DC_FF	100	0	80.6	16.9	2.5	0	23.2	54.7	22.1	99.9	0.01	100	0	100	0
5	DC_NC	100	0	100	0	0	0	100	0	0	100	0	99.4	0.06	87.4	12.6
6	DC_FiC	100	0	100	0	0	0	100	0	0	100	0	100	0	99.7	0.03
8	D&IC_NA	99.1	0.9	65.3	26.5	8.2	0	14.8	53.4	31.8	99.7	0.3	71.7	28.3	25.8	74.2
9	D&IC_FiA	99.1	0.9	62.5	28.8	8.7	0	15.4	53.9	30.7	99.6	0.4	68.1	31.9	22.1	77.9
10	D&IC_FF	98.7	1.3	60.1	29.6	9.9	0.4	14.4	53.8	31.8	99.5	0.5	63.3	36.7	19	81
11	D&IC_NC	98.7	1.3	64.2	28.5	7.3	0	18.6	58.2	23.2	99.6	0.4	66.9	33.1	19.6	80.4
12	D&IC_FiC	100	0	95.1	4.2	0.7	0	78.5	17.9	3.6	100	0	88.9	11.1	84.4	15.6

DC=Direct Contact, D&IC=Direct and indirect contact, NA=NurseryA, FiA=FinishingA, FF=Farrow-to-finish NC= NurseryC, FiC=FinishingC

Table S7 Descriptive summary of the predicted number of farms infected with PRRS virus and time required to reach the peak epidemic from simulation based on 1000 iterations of scenarios 13 and 19 (Set B scenarios)

Scenario No.	Scenario Name	Farms Infected: Median (p95)							Epidemic Size: Median (p95)			Week to peak epidemic (p95)
		Overall	Farrowing	NurseryA	FinishingA	Farrow-to-finish	NurseryC	FinishingC	Overall	NurseryA	FinishingA	
13.	DC_F	948 (1054)	1 (4)	86 (109)	489 (522)	0	40 (74)	333 (368)	1170 (1336)	104 (139)	689 (795)	37 (49)
19.	D&IC_F	1241 (1313)	13 (22)	165 (191)	547 (568)	10 (16)	124 (147)	382 (388)	1662 (1828)	257 (325)	875 (961)	27 (45)

DC=Direct Contact, D&IC=Direct and indirect contact, F=Farrowing

For median number of farms infected, farms that had multiple infections were counted only once; while for median epidemic size, farms with multiple outbreaks were counted multiple times. For Farrowing, Farrow-to -finish, NurseryC and FinishingC farms, the median epidemic sizes were similar to their respective median numbers of farms infected.

p95= 95th percentile

Table S8 Summary statistics relating to multiple outbreaks of PRRS virus during the period of simulation based on 1000 iterations of scenarios 13 and 19 (Set B scenarios)

Scenario No.	Scenario Name	Percentage of farms with the indicated number of outbreaks													
		Farrowing		NurseryA				FinishingA			Farrow-to-finish		NurseryC		FinishingC	
		0	1	0	1	2-3	>4	0	1	2-3	0	1	0	1	0	1
13	DC_F	99.7	0.3	68.5	25.6	5.9	0	18.1	51.2	30.7	100	0	78.1	21.9	15.7	84.3
19	D&IC_F	96.3	3.7	39.6	35.9	22.7	1.8	8.3	42.4	49.3	98.7	1.3	31.9	68.1	3.3	96.7

DC=Direct Contact, D&IC=Direct and indirect contact, F=Farrowing

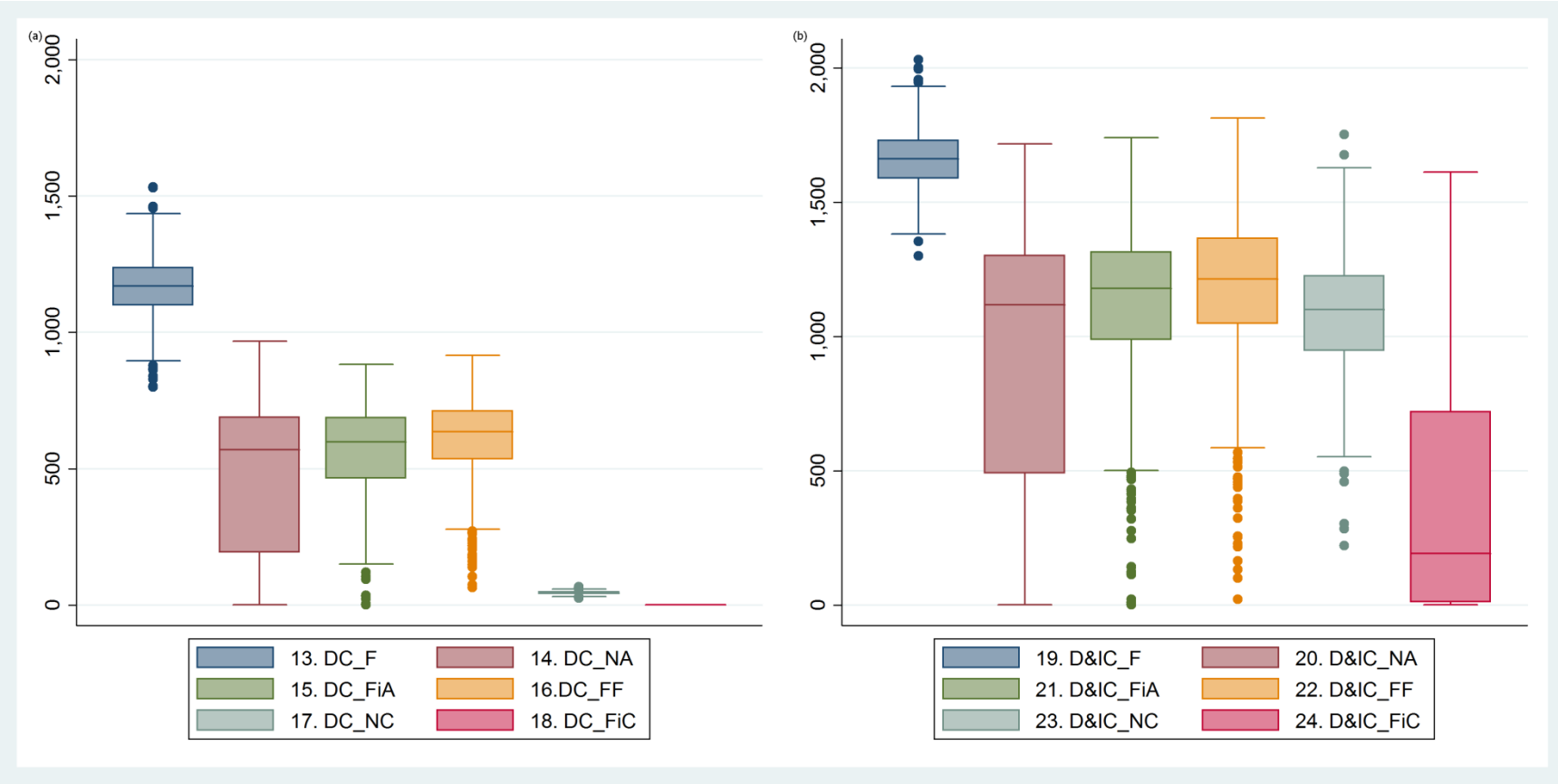


Figure S1 Distribution of the overall epidemic size of PRRS virus simulated outbreaks of between-farm spread among swine herds of Ontario under assumptions of direct (a) and direct and indirect contacts (b) between farms for Set B scenarios. Different colors represent outputs from scenarios in which the epidemic was initiated from farm of the noted production type. DC=Direct Contact, D&IC=Direct and indirect contact, F=Farrowing, NA=NurseryA, FiA=FinishingA, FF=Farrow-to-finish NC= NurseryC, FiC=FinishingC.

The middle band of the box represents 50th percentile, the bottom and top of the box represents 25th and 75th percentile and the end of the whiskers represent maximum and minimum within ±1.5 interquartile range of the epidemic size distribution.

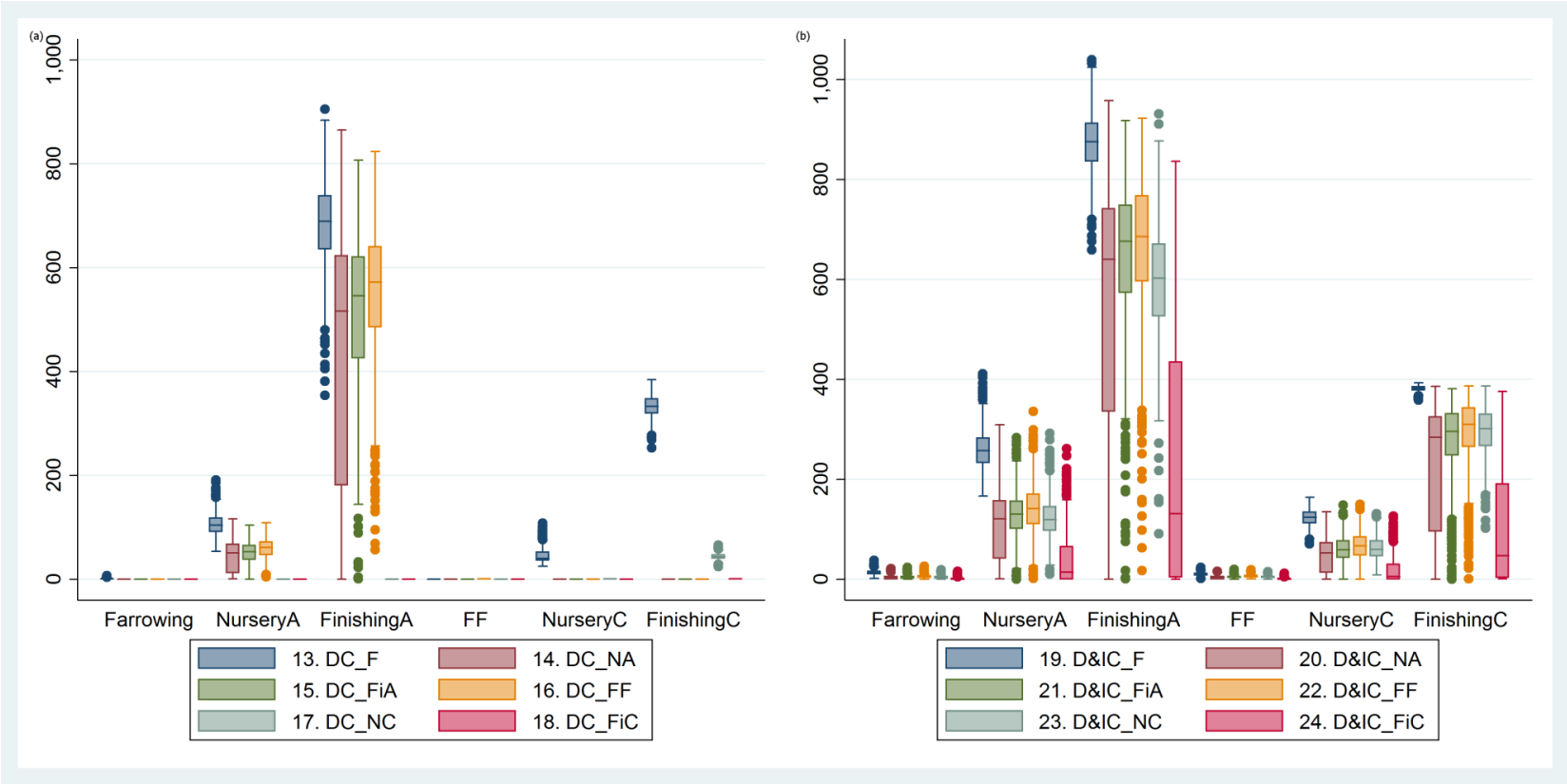


Figure S2 Distribution of epidemic size of PRRS virus simulated outbreaks by swine production type among swine herds of Ontario under assumptions of (a) direct and (b) direct and indirect contact between farms for Set B scenarios. Different colors represent scenarios in which farms of the indicated production type were the initially infected premises. DC=Direct Contact, D&IC=Direct and indirect contact, F=Farrowing, NA=NurseryA, FiA=FinishingA, FF=Farrow-to-finish NC= Nurseries, FiC=FinishingC.

The middle band of the box represents 50th percentile, the bottom and top of the box represents 25th and 75th percentile and the end of the whiskers represent maximum and minimum within ±1.5 interquartile range of the epidemic size distribution.

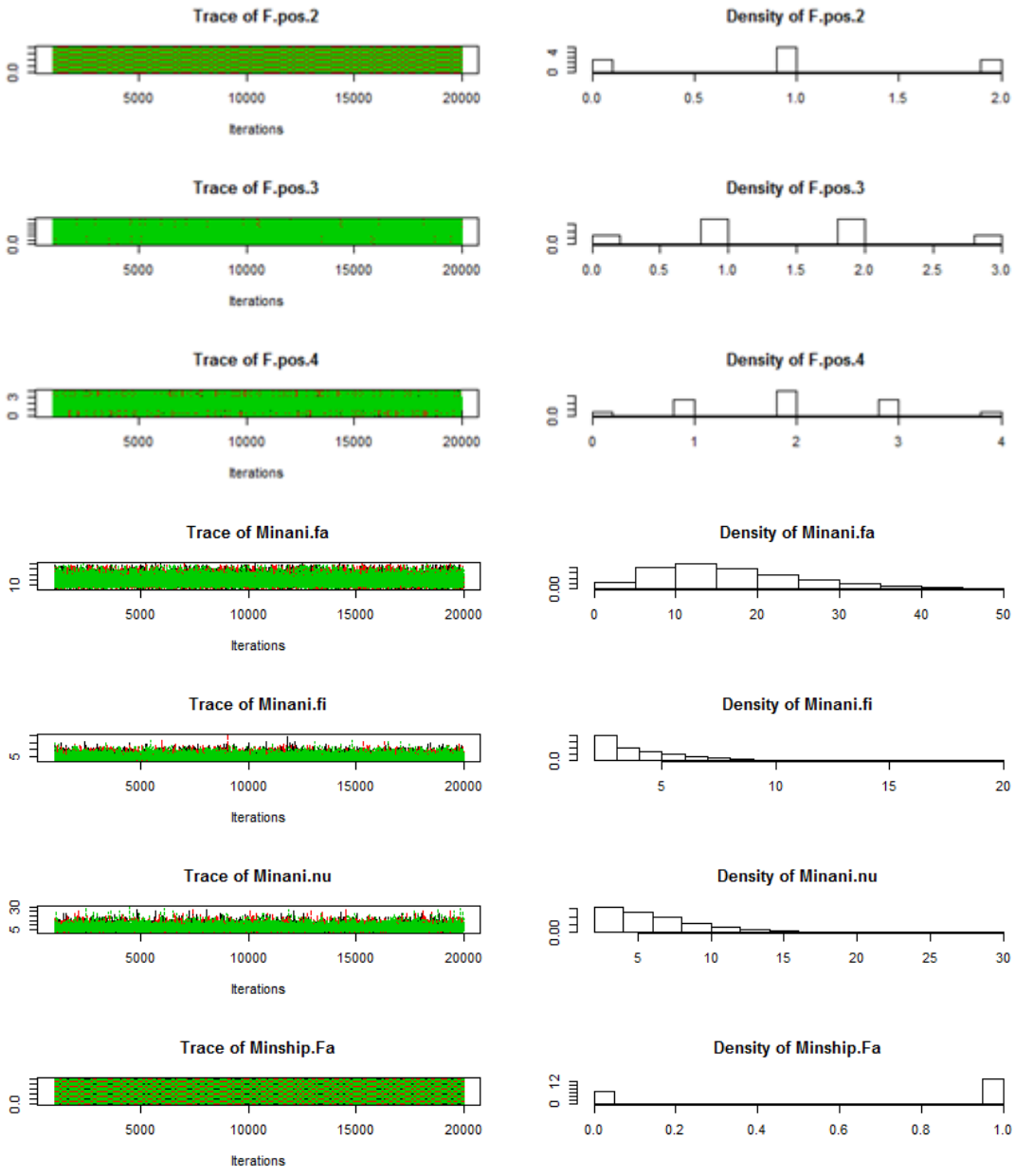
Table S9 Summary posterior distribution of nodes and scenarios used in the Bayesian model simulated to evaluate the probability that a truck will be infected with PRRS virus at the end of a working day.

Nodes	Mean	SD[!]	Median	95% CrI*
F.pos.2	1.00	0.71	1	0-2
F.pos.3	1.50	0.87	2	0-3
F.pos.4	2.00	1.0	2	0-4
F.inf.2	0.753	0.43	1	0-1
F.inf.3	0.873	0.33	1	0-1
F.inf.4	0.938	0.24	1	0-1
Comb.prob	0.833	0.23	1	0-1
Min_{ani}.Fa	17.15	9.05	16	4-39
Min_{ani}.Nu	6.47	3.31	6	2-15
Min_{ani}.Fi	4.34	2.00	4	2-9
Min_{ship}.Fa	0.667	0.47	1	0-1
Min_{ship}.Nu	0.688	0.46	1	0-1
Min_{ship}.Fi	0.699	0.46	1	1-1
Nani.Fa1	2.75	2.09	2	0-8
Nani.Nu1	2.58	1.81	2	0-7
Nani.Fi1	2.42	1.51	2	0-6
Nani.Fa1.step	0.688	0.46	1	0-1
Nani.Nu1.step	0.695	0.46	1	0-1
Nani.Nu1.step	0.710	0.45	1	0-1
Travel.time	2.43	0.90	2.42	0.685-4.22
Travel	0.678	0.47	1	0-1
W.efficacy	0.045	0.04	0.032	0.001-0.161
Wd.efficacy	0.583	0.13	0.588	0.308-0.831
Wdd.efficacy	0.917	0.07	0.939	0.716-0.998

Scenarios	Mean	SD[!]	Median	95% CrI*
S.2.fa	0.338	0.47	1	0-1
S.2.nu	0.349	0.48	1	0-1
S.2.fi	0.352	0.48	1	0-1
S.3.fa	0.395	0.49	1	0-1
S.3.nu	0.407	0.49	1	0-1
S.3.fi	0.413	0.49	1	0-1
S.4.fa	0.425	0.49	1	0-1
S.4.nu	0.438	0.50	1	0-1
S.4.fi	0.444	0.50	1	0-1
S.fa	0.377	0.44	1	0-1
S.nu	0.389	0.44	1	0-1
S.fi	0.394	0.44	1	0-1
S. fa.w	0.360	0.42	0	0-0.996
S.nu.w	0.371	0.43	0	0-0.996
S.fi.w	0.376	0.43	0	0-0.996
S.fa.wd	0.157	0.20	0	0-0.606
S.nu.wd	0.162	0.20	0	0-0.608
S.fi.wd	0.163	0.20	0	0-0.607
S.fa.wdd	0.031	0.06	0	0-0.202
S.nu.wdd	0.032	0.06	0	0-0.204
S.fi.wdd	0.033	0.06	0	0-0.204

[!]Standard deviation

*95% credible interval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Density of F.pos.2
Trace of F.pos.3
Density of F.pos.3
Trace of F.pos.4
Density of F.pos.4
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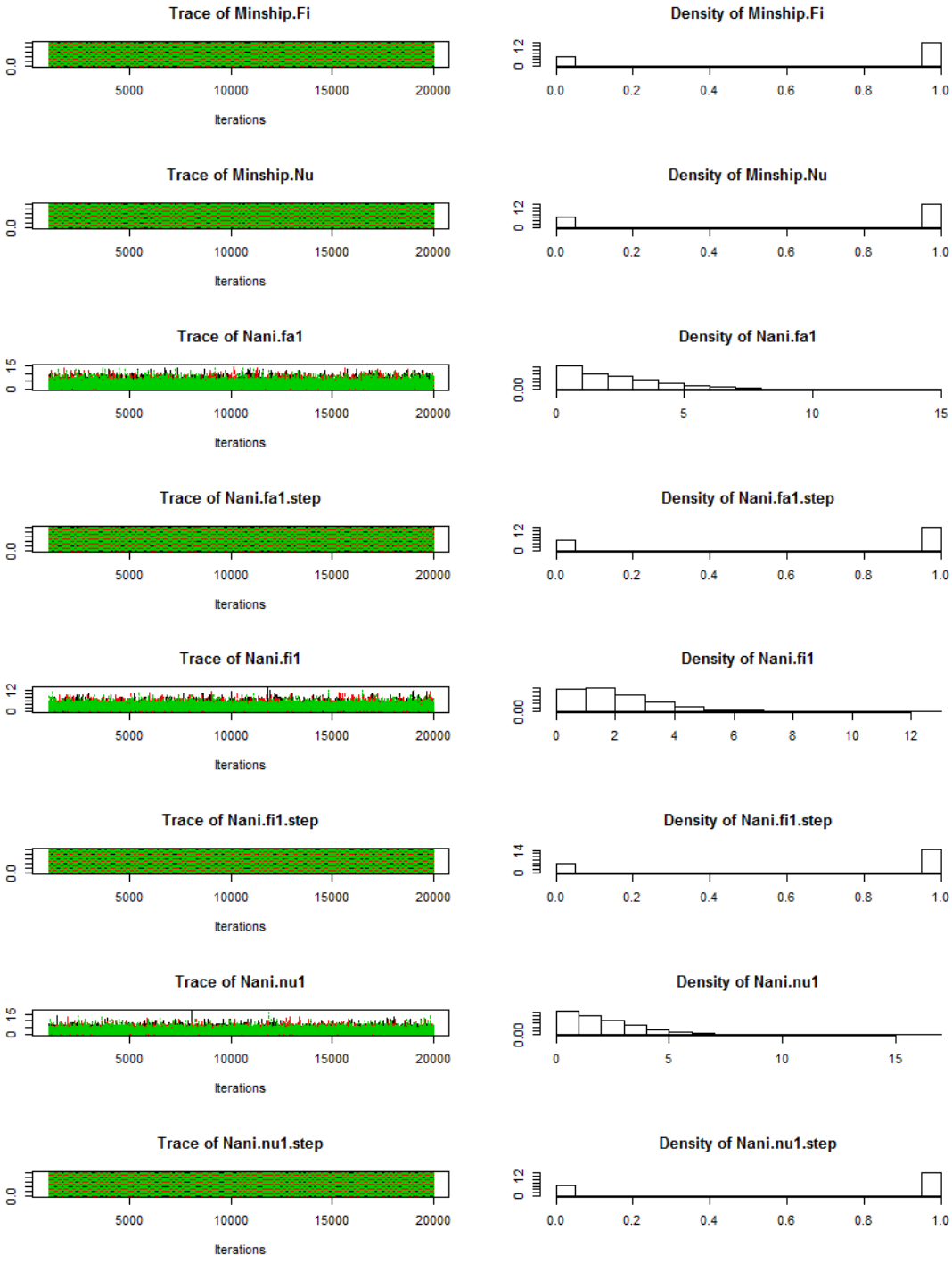
Density of Minani.fa
Trace of Minani.fi
Density of Minani.fi
Trace of Minani.nu
Density of Minani.nu
Trace of Minship.Fa
Density of Minship.Fa
Iterations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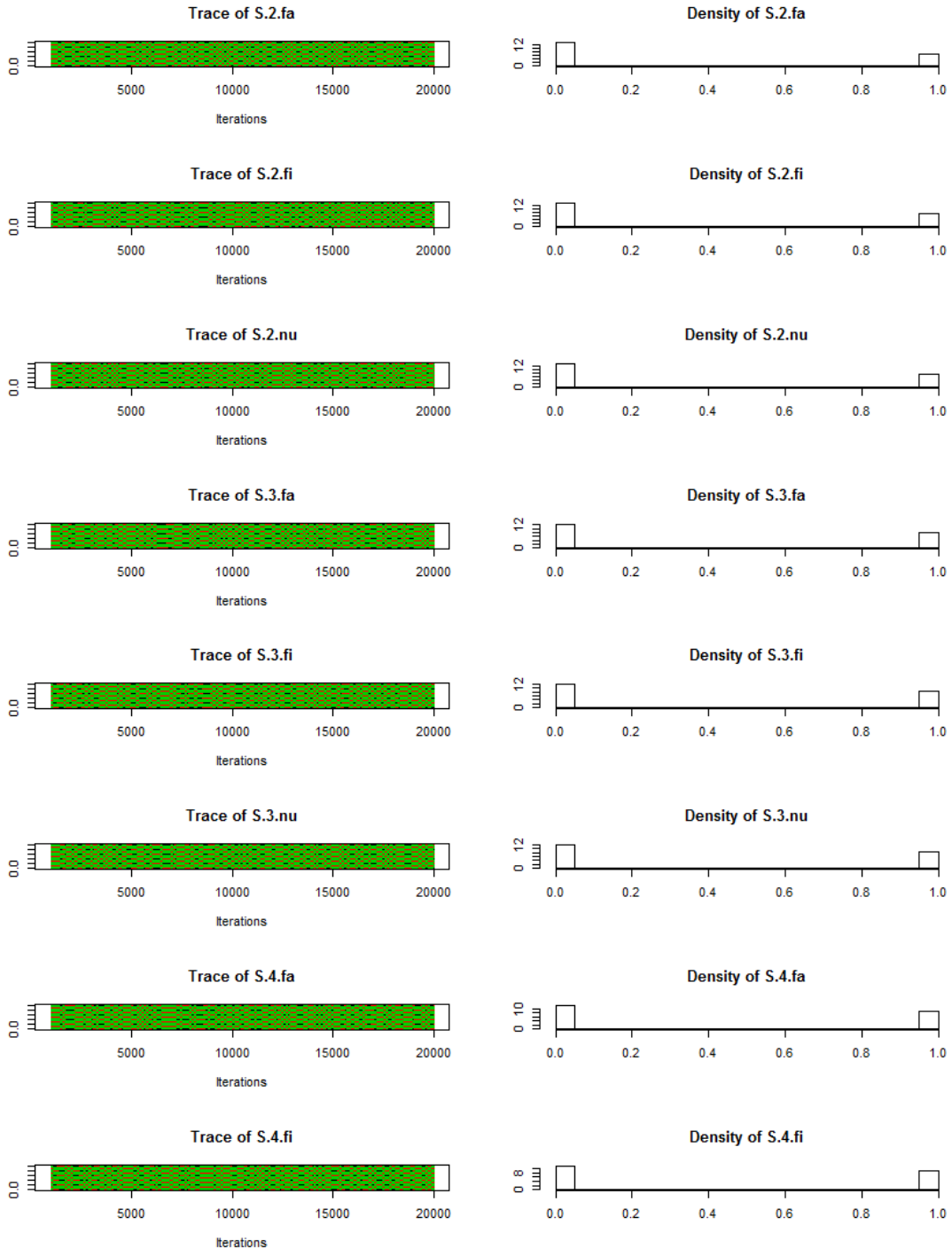
Iterations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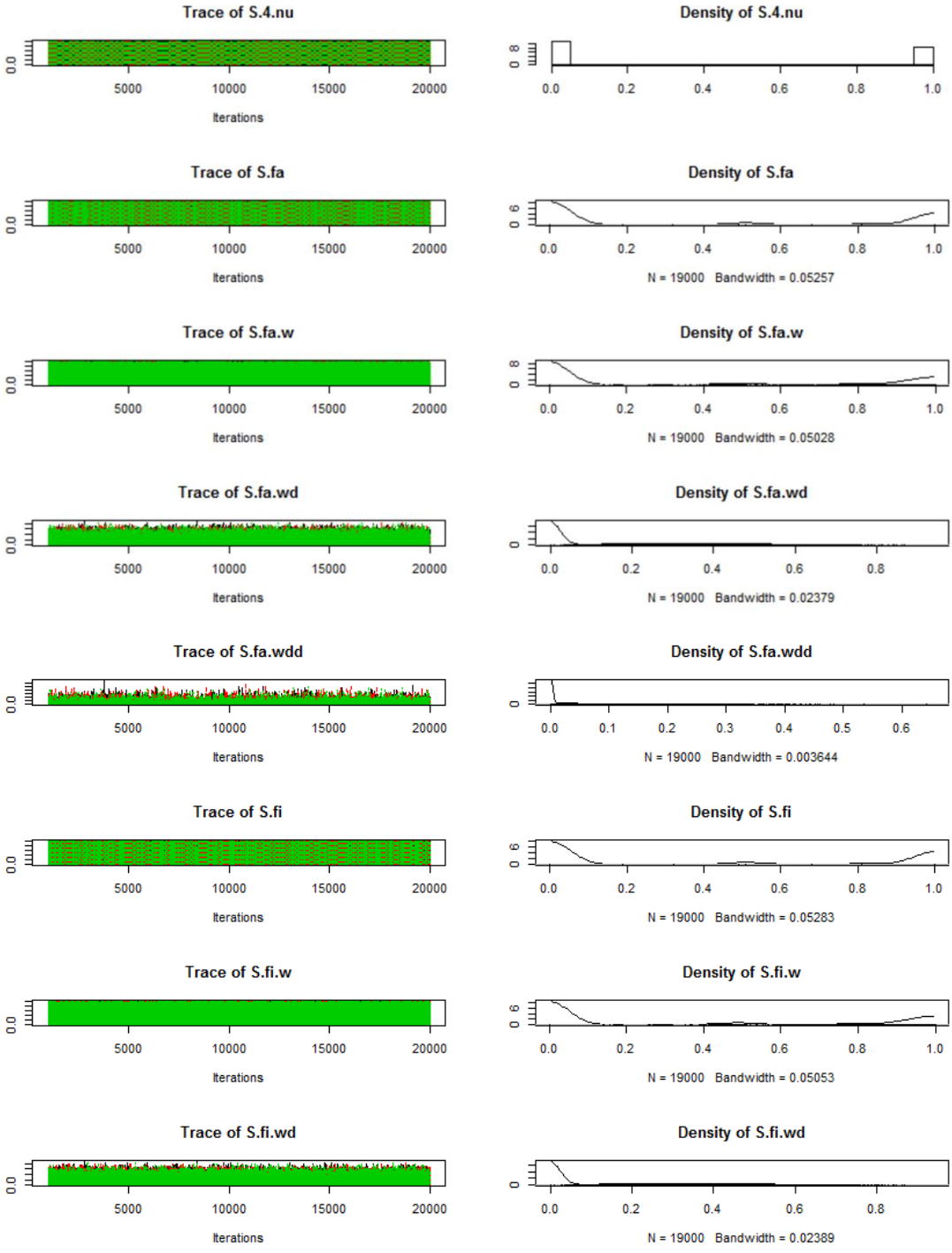
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Trace of S.fa
Density of S.fa
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Density of S.fi
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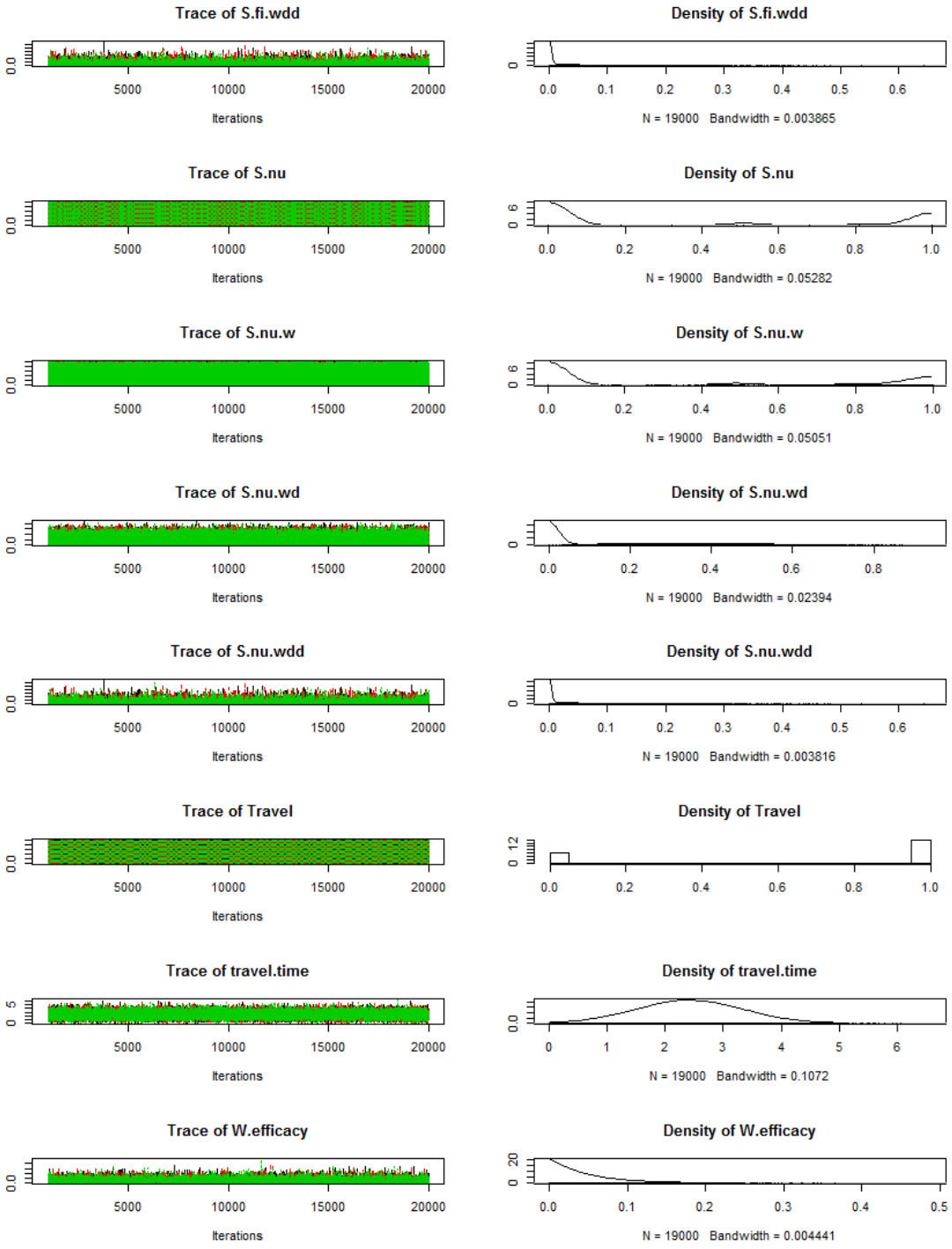
Iterations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Iterations
Density of S.fi.wdd
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Trace of S.nu
Iterations
Density of S.nu
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Trace of S.nu.w
Iterations
Density of S.nu.w
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Iterations
Density of S.nu.wd
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Iterations
Density of S.nu.wdd
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Density of Travel
Trace of travel.time
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Iterations
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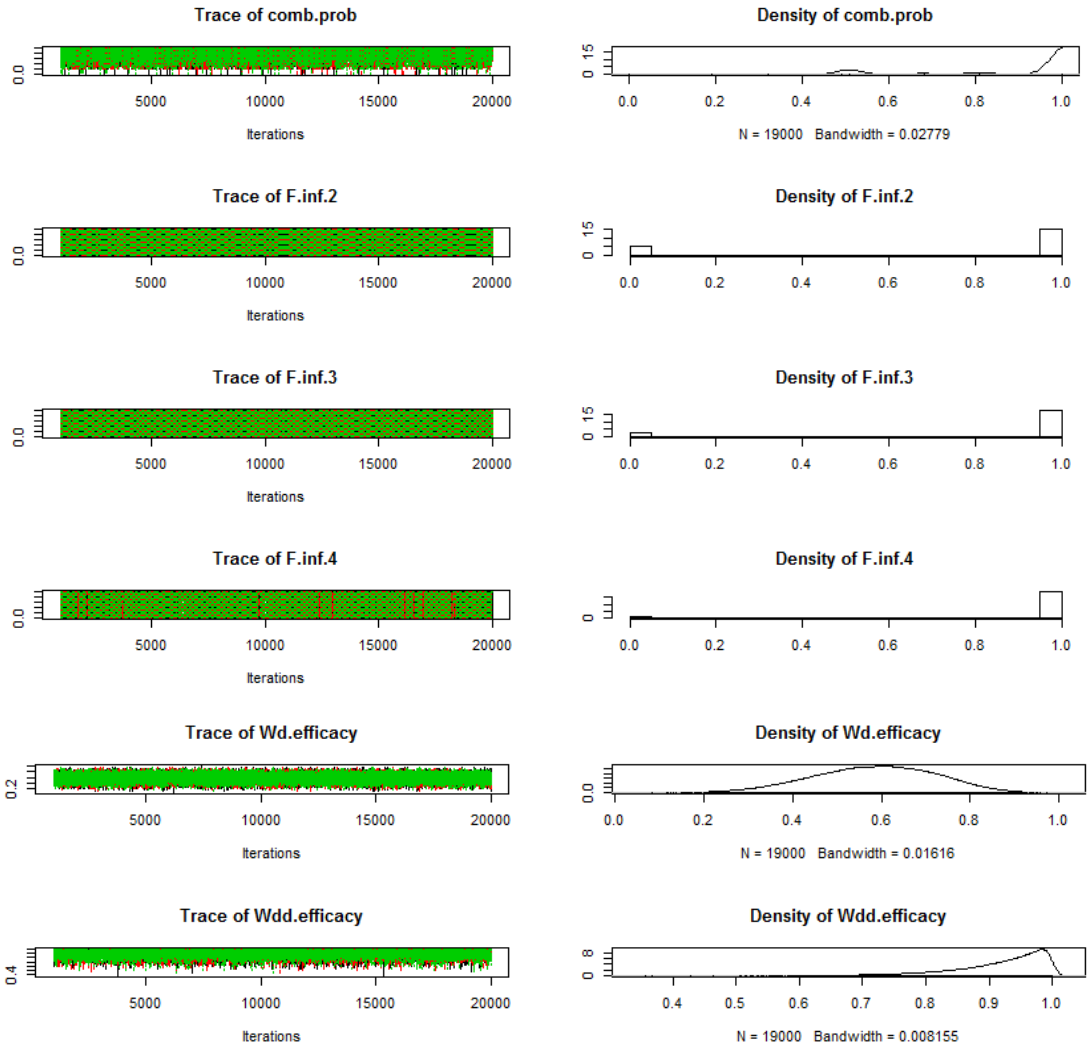
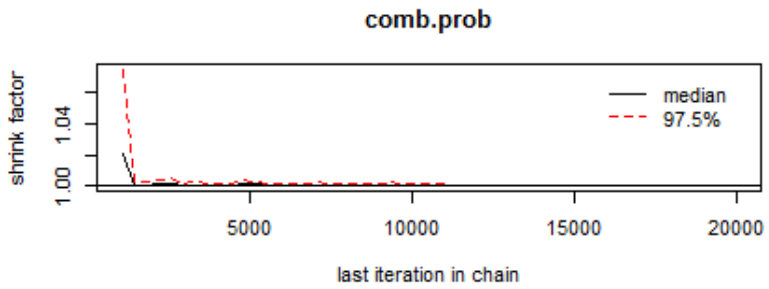


Figure S3 History and density plots, generated with three initial chains, for all the parameters and scenarios simulated to estimate the probability that the truck is contaminated with PRRS virus at the end of Day 1.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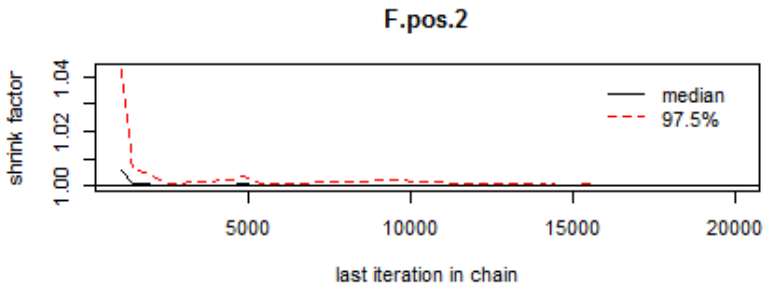
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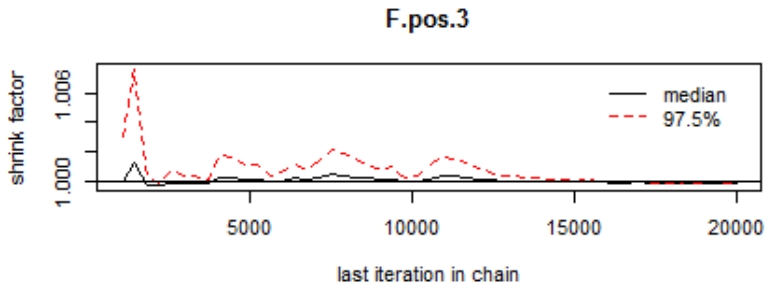
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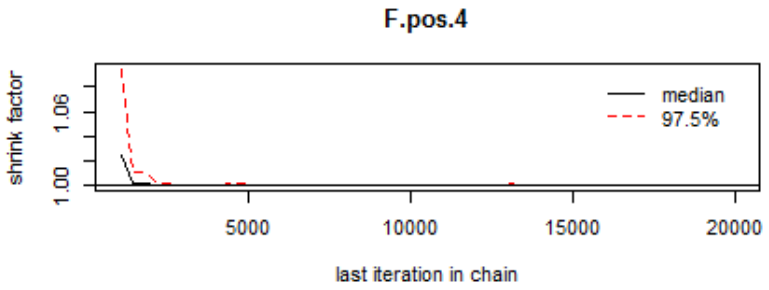
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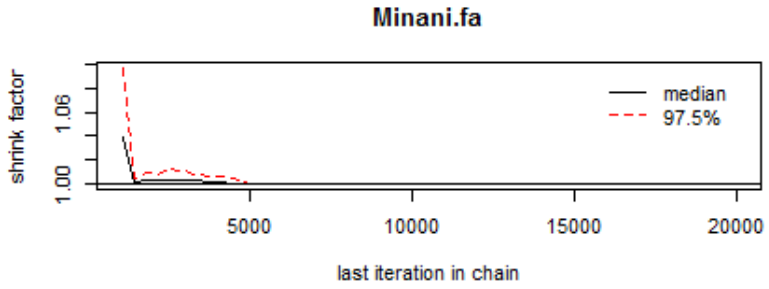
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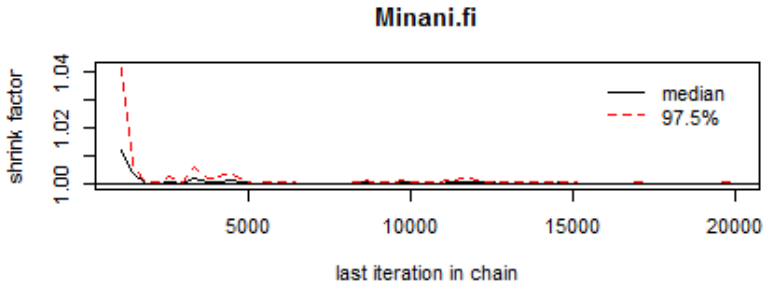
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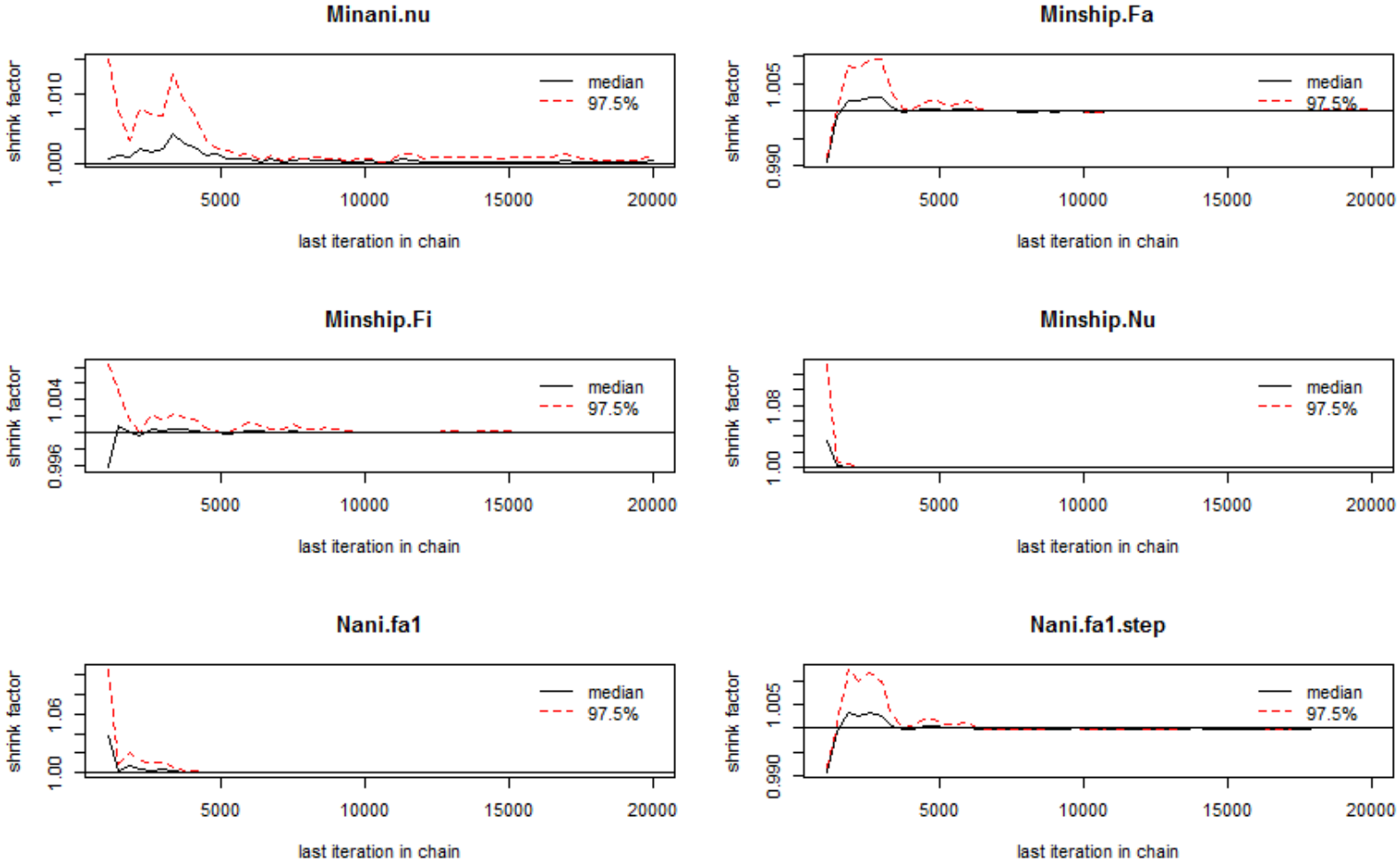
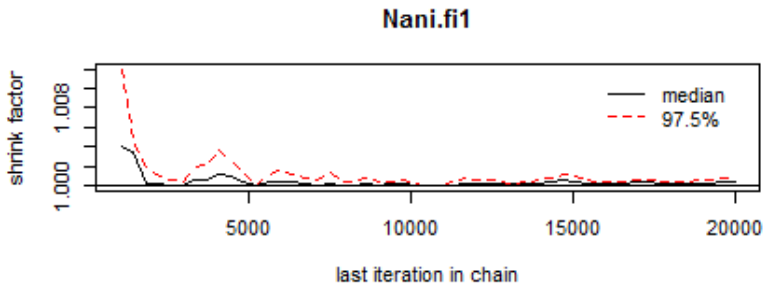
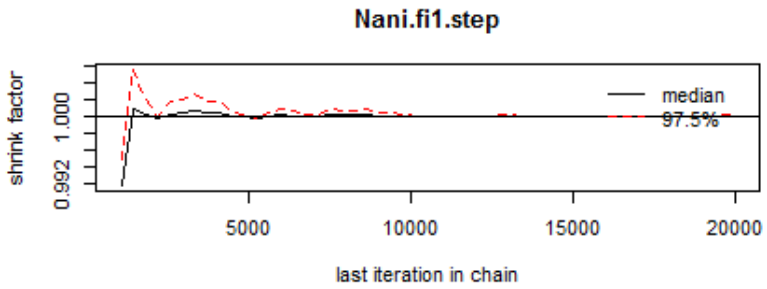
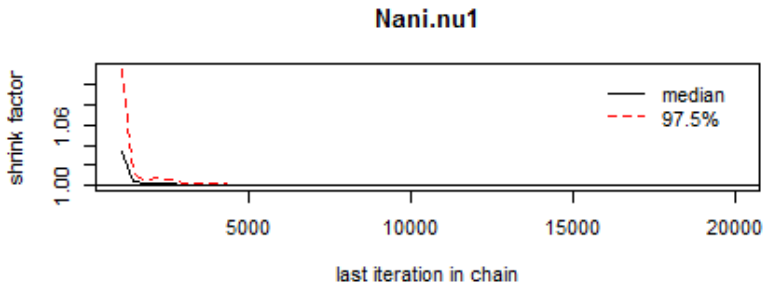
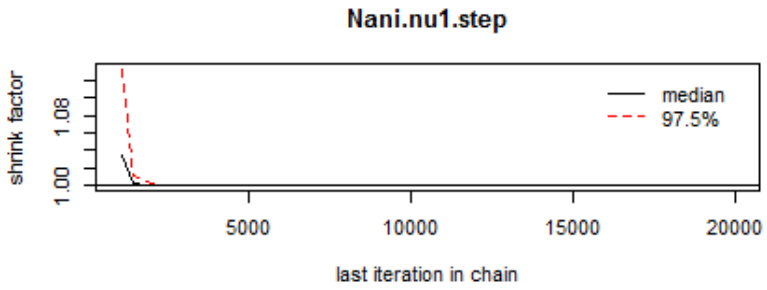
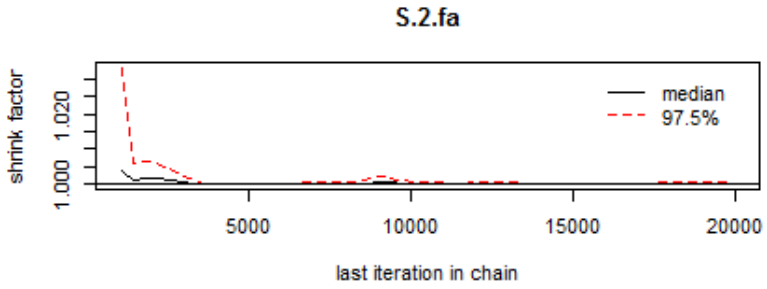

Minani.nu
shrink factor
1.000
1.010
median
97.5%
5000
10000
15000
20000
last iteration in chain
Minship.Fa
shrink factor
0.990
1.005
median
97.5%
5000
10000
15000
20000
last iteration in chain
Minship.Fi
shrink factor
0.996
1.004
median
97.5%
5000
10000
15000
20000
last iteration in chain
Minship.Nu
shrink factor
1.00
1.08
median
97.5%
5000
10000
15000
20000
last iteration in chain
Nani.fa1
shrink factor
1.00
1.06
median
97.5%
5000
10000
15000
20000
last iteration in chain
Nani.fa1.step
shrink factor
0.990
1.005
median
97.5%
5000
10000
15000
20000
last iteration in chain

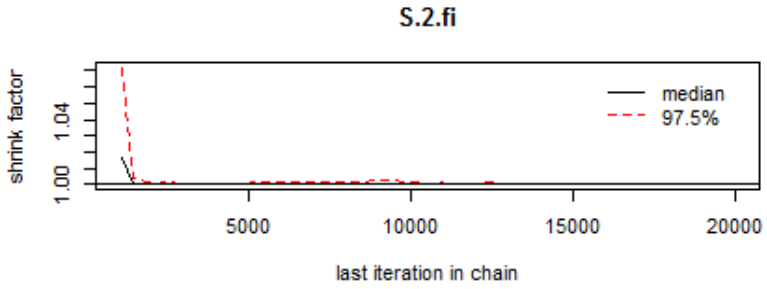

Nani.fi1
shrink factor
1.000
1.008
median
97.5%
5000
10000
15000
20000
last iteration in chain

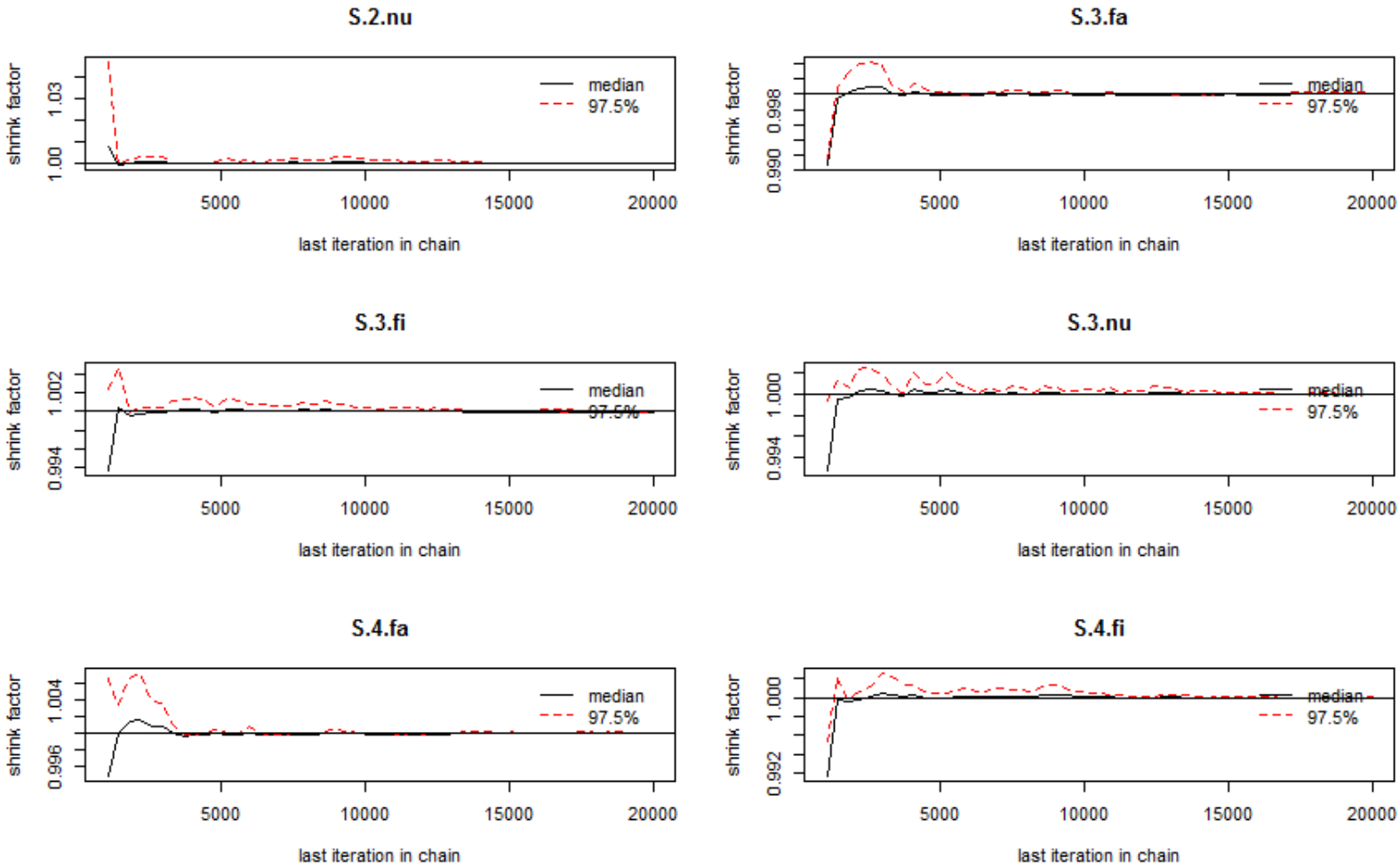

Nani.fi1.step
shrink factor
0.992
1.000
median
97.5%
5000
10000
15000
20000
last iteration in chain

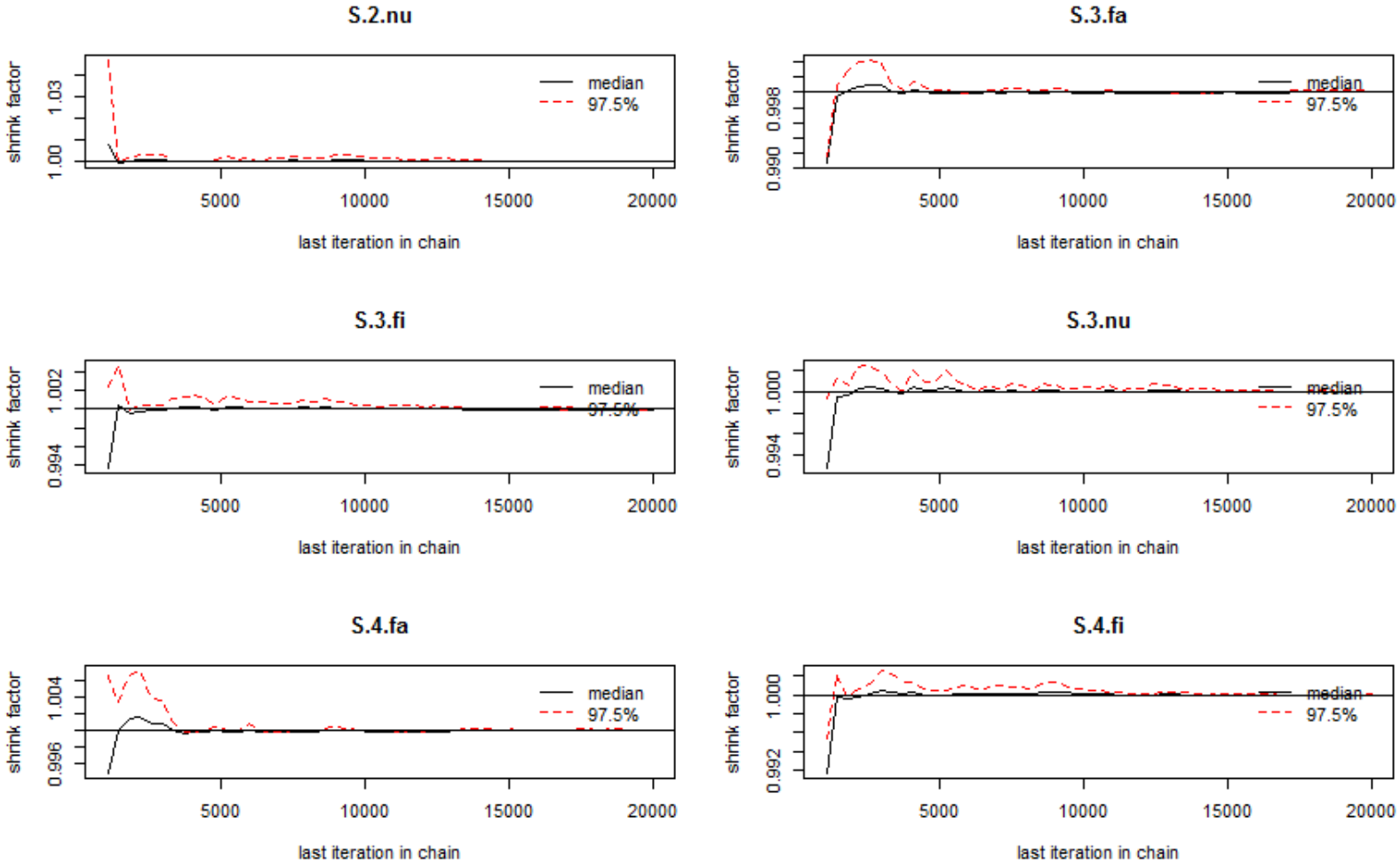

Nani.nu1
shrink factor
1.00
1.06
median
97.5%
5000
10000
15000
20000
last iteration in chain

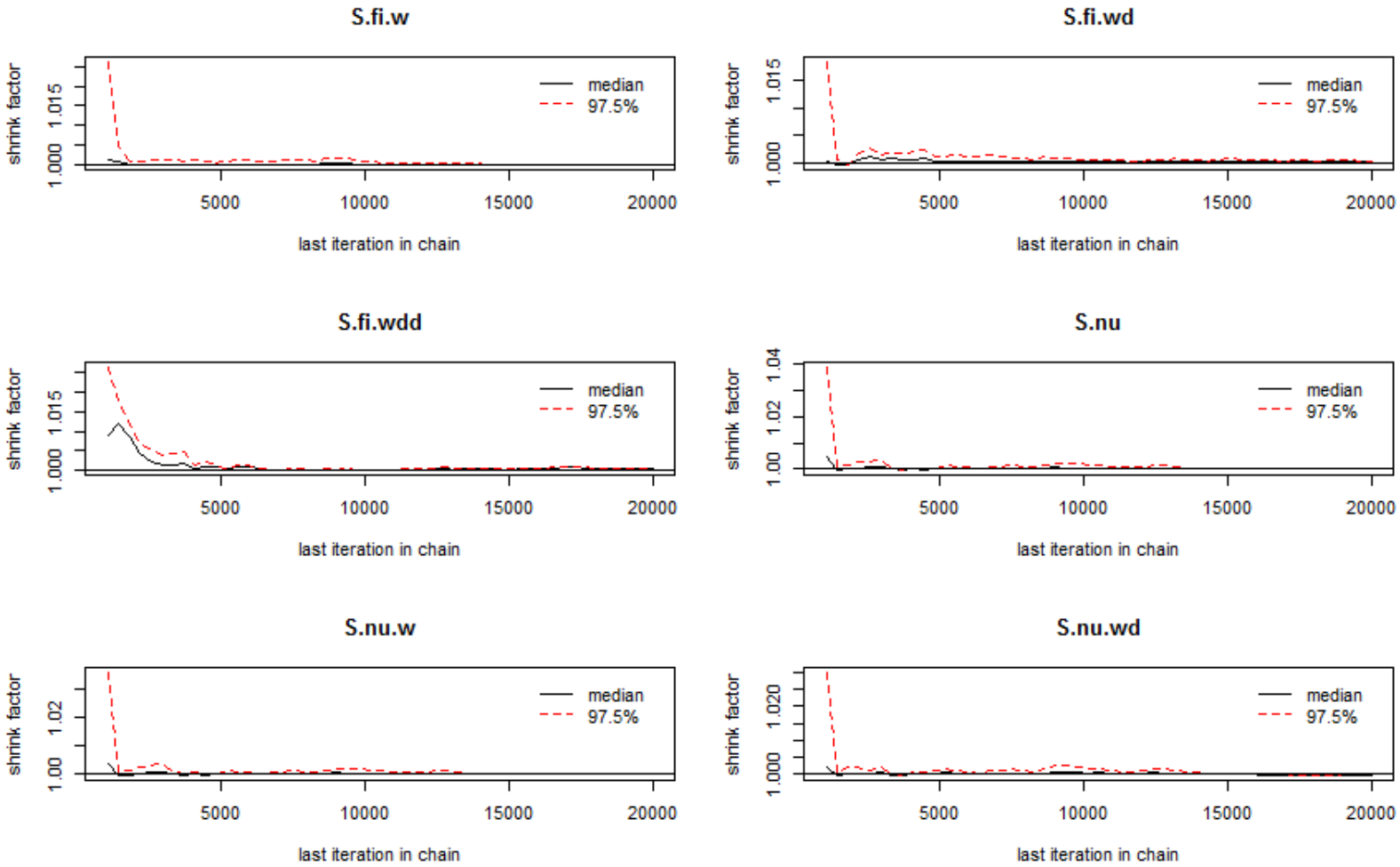

Nani.nu1.step
shrink factor
1.00
1.08
median
97.5%
5000
10000
15000
20000
last iteration in chain

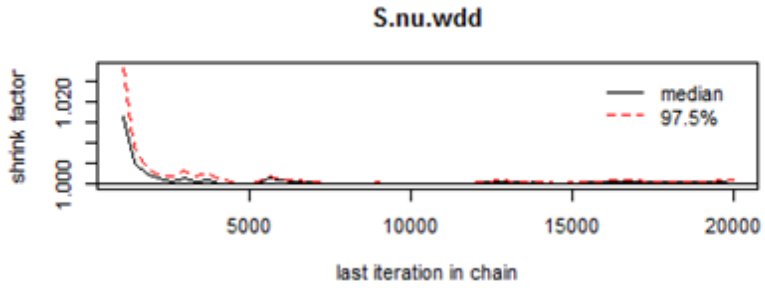

S.2.fa
shrink factor
1.000
1.020
median
97.5%
5000
10000
15000
20000
last iteration in chain

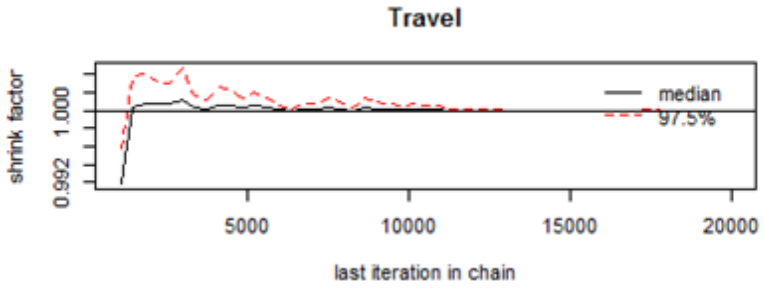

S.2.fi
shrink factor
1.00
1.04
median
97.5%
5000
10000
15000
20000
last iteration in chain

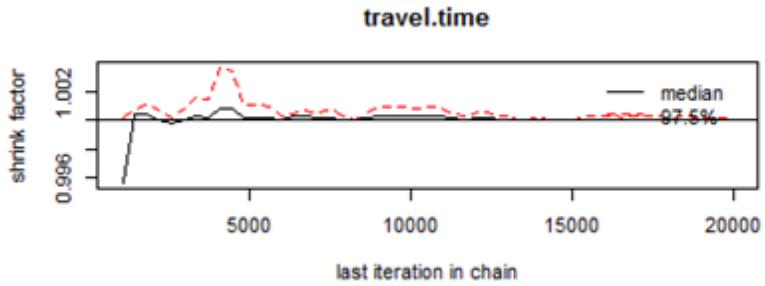

S.2.nu
shrink factor
1.00
1.03
median
97.5%
5000
10000
15000
20000
last iteration in chain
S.3.fa
shrink factor
0.990
0.998
median
97.5%
5000
10000
15000
20000
last iteration in chain
S.3.fi
shrink factor
0.994
1.002
median
97.5%
5000
10000
15000
20000
last iteration in chain
S.3.nu
shrink factor
0.994
1.000
median
97.5%
5000
10000
15000
20000
last iteration in chain
S.4.fa
shrink factor
0.996
1.004
median
97.5%
5000
10000
15000
20000
last iteration in chain
S.4.fi
shrink factor
0.992
1.000
median
97.5%
5000
10000
15000
20000
last iteration in chain

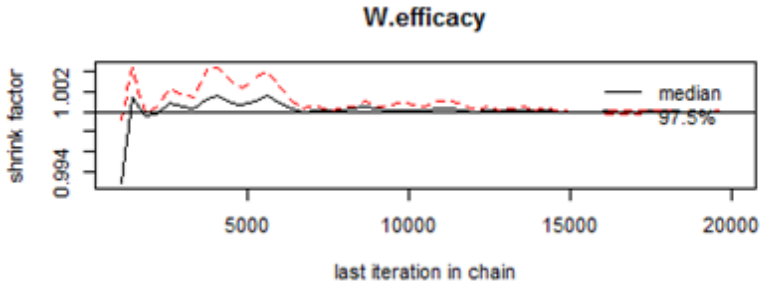

S.2.nu
shrink factor
1.00
1.03
median
97.5%
5000
10000
15000
20000
last iteration in chain
S.3.fa
shrink factor
0.990
0.998
median
97.5%
5000
10000
15000
20000
last iteration in chain
S.3.fi
shrink factor
0.994
1.002
median
97.5%
5000
10000
15000
20000
last iteration in chain
S.3.nu
shrink factor
0.994
1.000
median
97.5%
5000
10000
15000
20000
last iteration in chain
S.4.fa
shrink factor
0.996
1.004
median
97.5%
5000
10000
15000
20000
last iteration in chain
S.4.fi
shrink factor
0.992
1.000
median
97.5%
5000
10000
15000
20000
last iteration in chain


S.fi.w
shrink factor
1.000
1.015
median
97.5%
5000
10000
15000
20000
last iteration in chain
S.fi.wd
shrink factor
1.000
1.015
median
97.5%
5000
10000
15000
20000
last iteration in chain
S.fi.wdd
shrink factor
1.000
1.015
median
97.5%
5000
10000
15000
20000
last iteration in chain
S.nu
shrink factor
1.00
1.02
1.04
median
97.5%
5000
10000
15000
20000
last iteration in chain
S.nu.w
shrink factor
1.00
1.02
median
97.5%
5000
10000
15000
20000
last iteration in chain
S.nu.wd
shrink factor
1.000
1.020
median
97.5%
5000
10000
15000
20000
last iteration in chain


S.nu.wdd
shrink factor
1.000
1.020
median
97.5%
5000
10000
15000
20000
last iteration in chain


Travel
shrink factor
0.992
1.000
median
97.5%
5000
10000
15000
20000
last iteration in chain


travel.time
shrink factor
0.996
1.002
median
97.5%
5000
10000
15000
20000
last iteration in chain


W.efficacy
shrink factor
0.994
1.002
median
97.5%
5000
10000
15000
20000
last iteration in chain

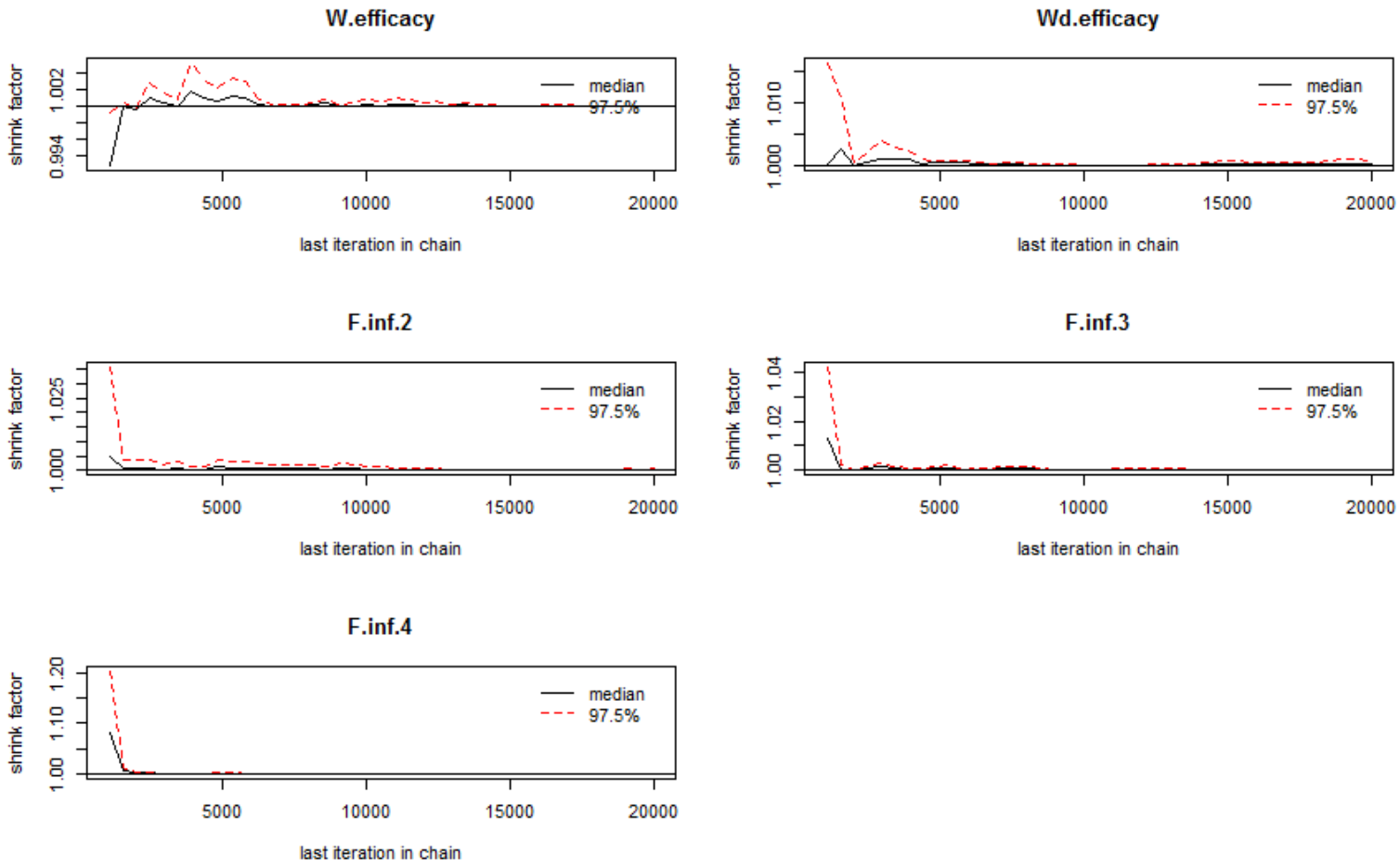
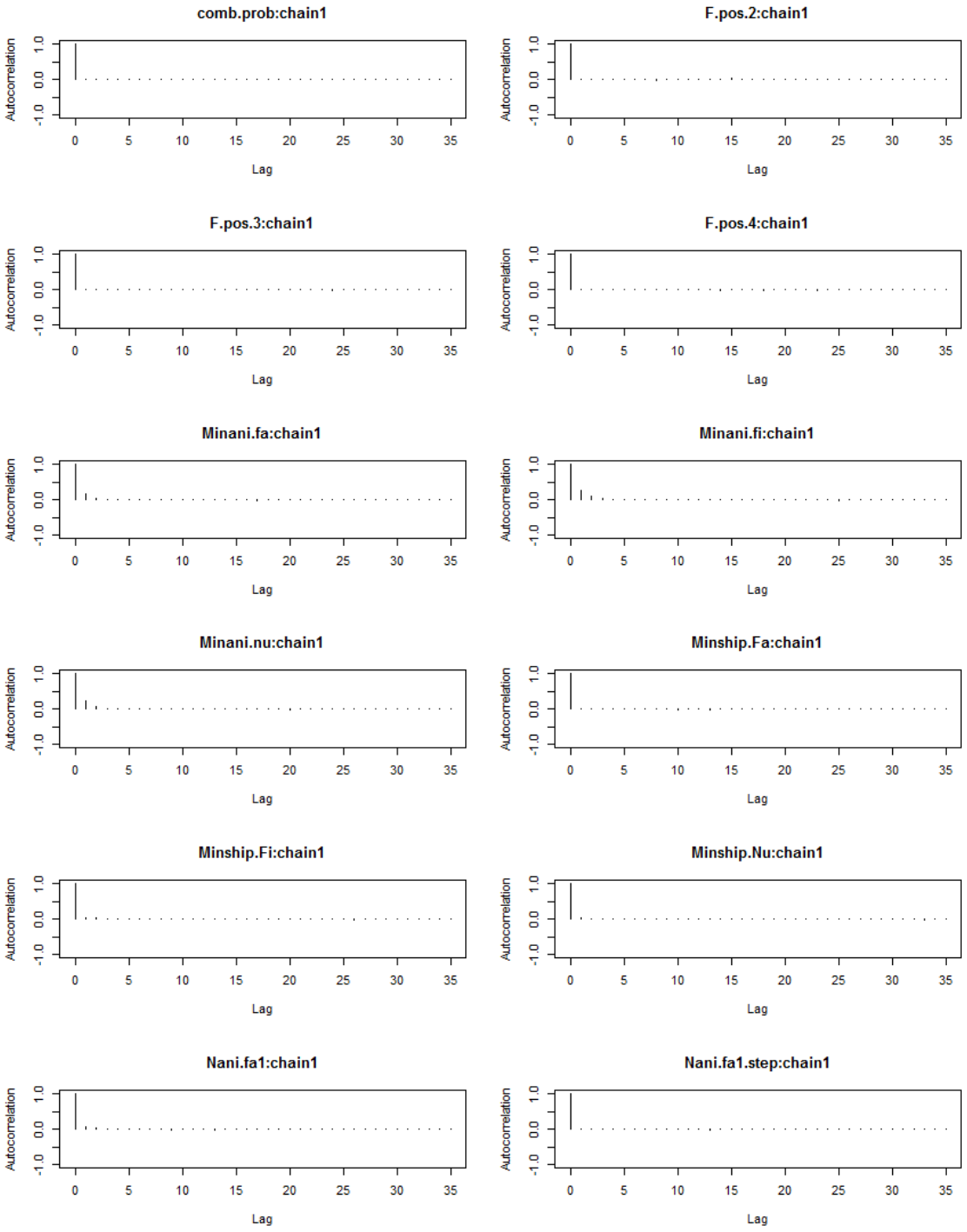
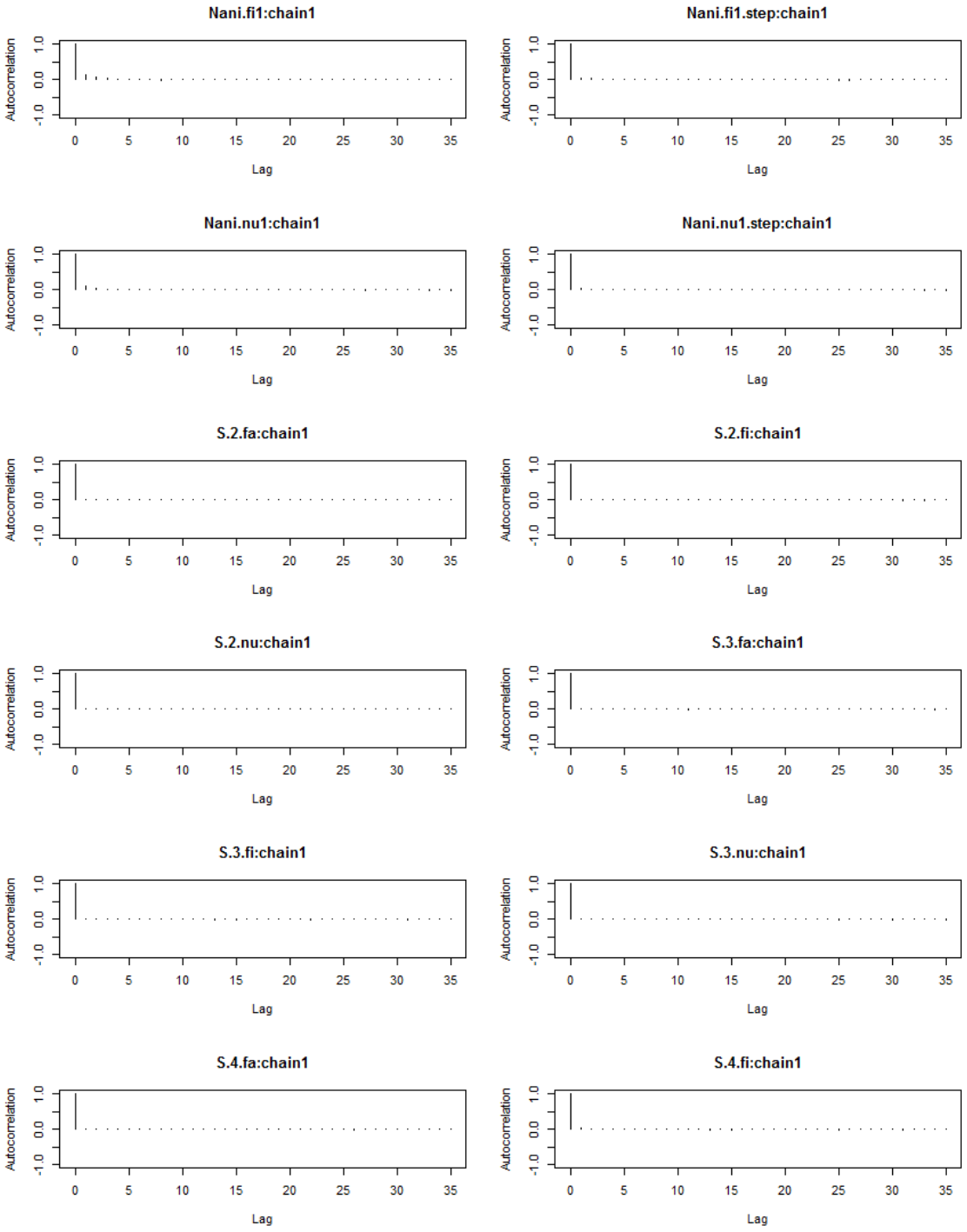
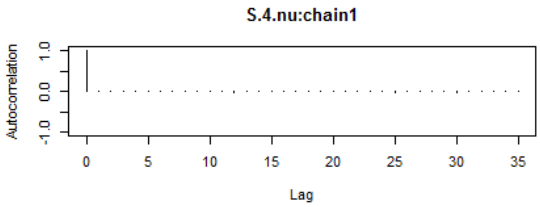
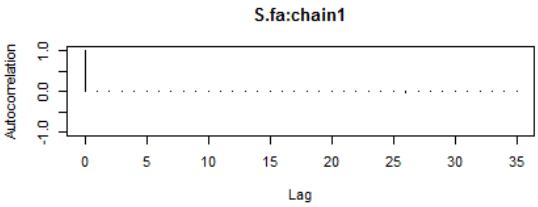


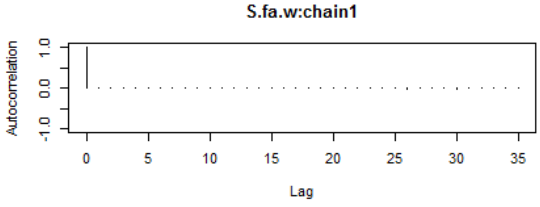
Figure S4 Shrinkage (Gelman) plots of median scale reduction factor and 97.5% upper bounds, generated with three initial chains to evaluate evolution of scale-reduction factor with increase in number of iterations, for all the parameters and scenarios simulated to estimate the probability that the truck is contaminated with PRRS virus at the end of Day 1.

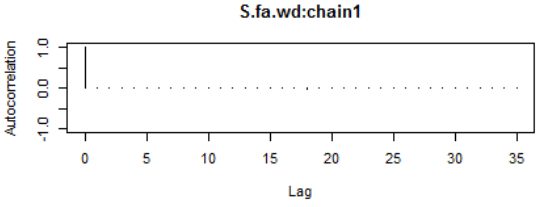

comb.prob:chain1
F.pos.2:chain1
F.pos.3:chain1
F.pos.4:chain1
Minani.fa:chain1
Minani.fi:chain1
Minani.nu:chain1
Minship.Fa:chain1
Minship.Fi:chain1
Minship.Nu:chain1
Nani.fa1:chain1
Nani.fa1.step:chain1
Autocorrelation
Lag

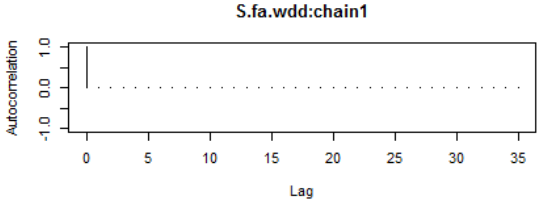

Nani.fi1:chain1
Nani.fi1.step:chain1
Nani.nu1:chain1
Nani.nu1.step:chain1
S.2.fa:chain1
S.2.fi:chain1
S.2.nu:chain1
S.3.fa:chain1
S.3.fi:chain1
S.3.nu:chain1
S.4.fa:chain1
S.4.fi:chain1
Autocorrelation
-1.0
0.0
1.0
0
5
10
15
20
25
30
35
Lag

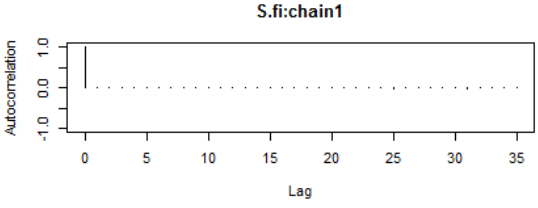

S.4.nu:chain1
Autocorrelation
-1.0 0.0 1.0
0 5 10 15 20 25 30 35
Lag

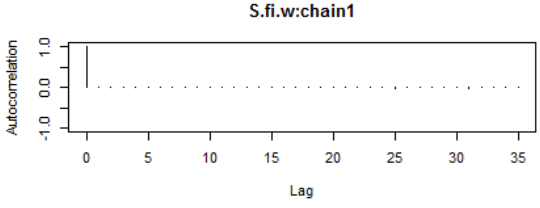

S.fa:chain1
Autocorrelation
-1.0 0.0 1.0
0 5 10 15 20 25 30 35
Lag

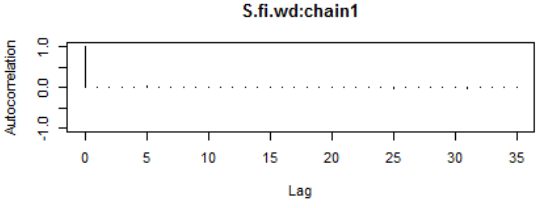

S.fa.w:chain1
Autocorrelation
-1.0 0.0 1.0
0 5 10 15 20 25 30 35
Lag

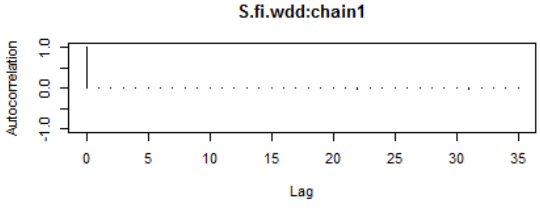

S.fa.wd:chain1
Autocorrelation
-1.0 0.0 1.0
0 5 10 15 20 25 30 35
Lag

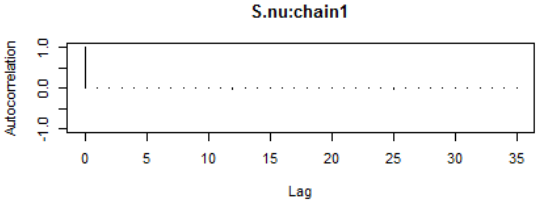

S.fa.wdd:chain1
Autocorrelation
-1.0 0.0 1.0
0 5 10 15 20 25 30 35
Lag

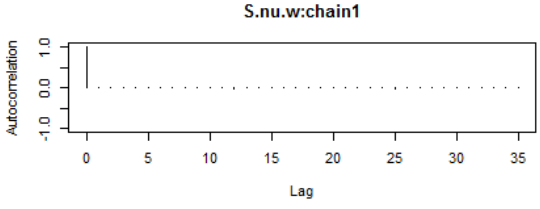

S.fi:chain1
Autocorrelation
-1.0 0.0 1.0
0 5 10 15 20 25 30 35
Lag

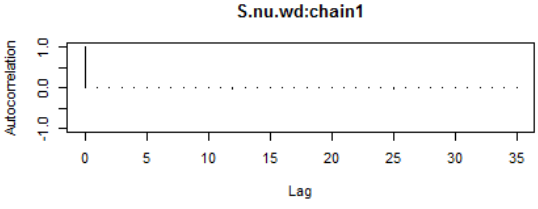

S.fi.w:chain1
Autocorrelation
-1.0 0.0 1.0
0 5 10 15 20 25 30 35
Lag


S.fi.wd:chain1
Autocorrelation
-1.0 0.0 1.0
0 5 10 15 20 25 30 35
Lag


S.fi.wdd:chain1
Autocorrelation
-1.0 0.0 1.0
0 5 10 15 20 25 30 35
Lag


S.nu:chain1
Autocorrelation
-1.0 0.0 1.0
0 5 10 15 20 25 30 35
Lag


S.nu.w:chain1
Autocorrelation
-1.0 0.0 1.0
0 5 10 15 20 25 30 35
Lag


S.nu.wd:chain1
Autocorrelation
-1.0 0.0 1.0
0 5 10 15 20 25 30 35
Lag

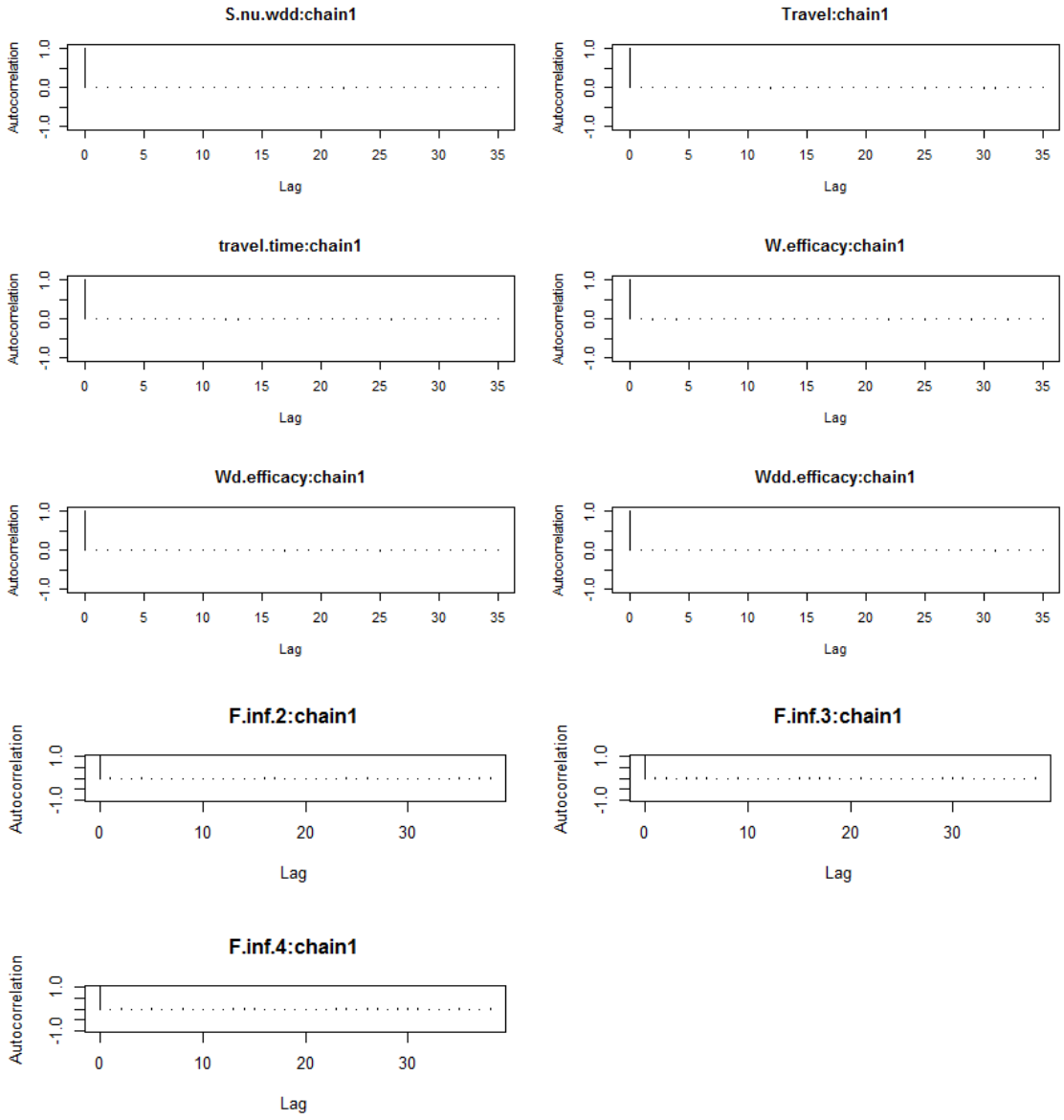


Figure S5 Autocorrelation plots for all the parameters and scenarios simulated to estimate the probability that the truck is contaminated with PRRS virus at the end of Day 1.